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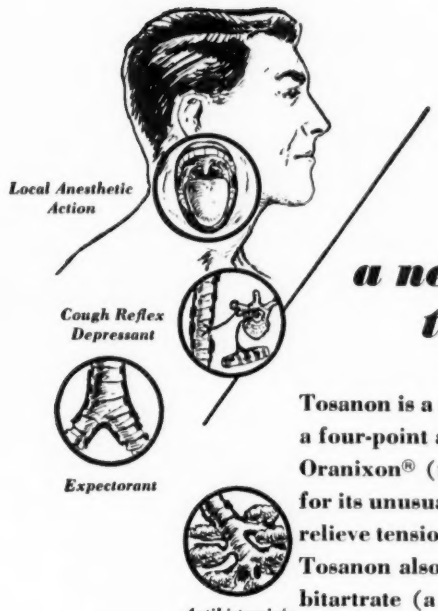

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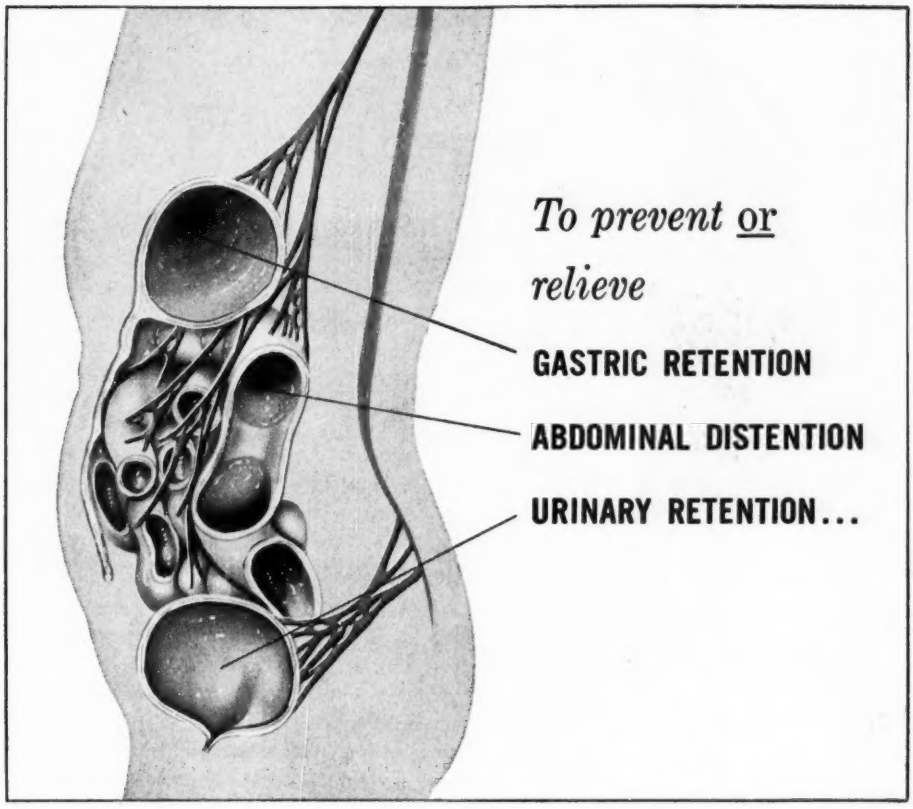

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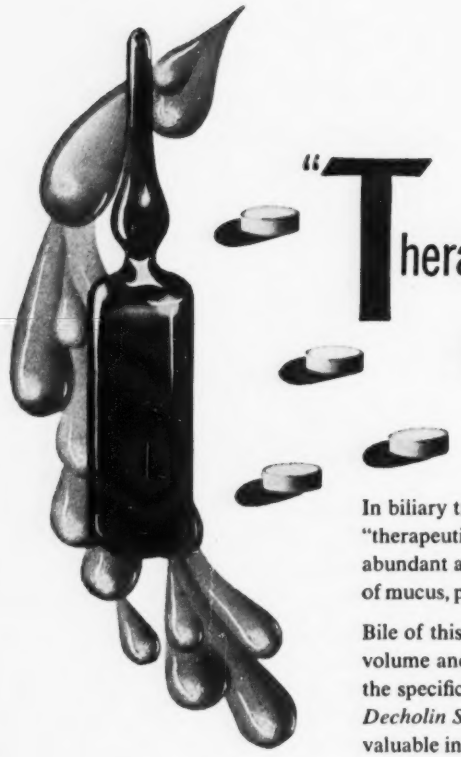

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MULTIPLE PRIMARY CARCINOMAS OF THE SMALL INTESTINE: A REVIEW OF THE LITERATURE

MAURICE FELDMAN, M. D., Baltimore Maryland.

THE INCIDENCE of carcinoma of the small intestine is extremely low. The necropsy incidence is about 0.5 per cent (7). In a collected group of 197,293 autopsies and surgical specimens (4, 12, 14, 15) there were sixty-three cases of carcinoma of the small intestine, an incidence of 0.03 per cent.

Multiple carcinomata are noted more often in the stomach and colon than elsewhere in the gastrointestinal tract. Multiple growths are more commonly observed in the colon than in the small intestine. When one organ is affected the colon is the most frequent site for multiple carcinomata. The low incidence of carcinoma of the small intestine and the rarity of multiple lesions in this portion of the intestinal tract has been commented upon by many observers. The extremely low incidence of multiple carcinomas of the small intestine accounts for the paucity of literature on this subject. Multiple carcinomas of the small intestine are not described in many textbooks of surgery and pathology. Feldman (7) mentions the condition in his textbook. In order to determine how often multiple carcinomas occur in the small intestine a survey of the literature was undertaken.

In this study only primary carcinomas were considered. Secondary carcinomas, metastases, and carcinomas originating from benign tumors or carcinoids were excluded from this survey. The purpose of this presentation is to review the literature, document the recorded cases and bring the number of cases of multiple carcinomata of the small intestine up to date. In this review one is struck by the paucity of literature on this subject. There are but few reports pertaining to primary multiple carcinomas of the small intestine. There are fewer cases of multiple cancers limited to the small bowel than in any other portion of the gastrointestinal tract. The condition is so rare that most surgeons and pathologists have not seen a single case in their many years of practice. In the Department of Pathology of the Sinai Hospital there were no cases of primary multiple carcinomas of the small intestine among 1,082 adult autopsies.* It must be emphasized that multiple lesions in the small bowel and/or in the small bowel associated with lesions elsewhere in the gastrointestinal tract must be especially sought after, otherwise they may elude discovery. However, it is not at all likely that these cases are being overlooked at autopsy because of the usual routine thoroughness with which the examination is carried out. On the other hand, they may be overlooked and often are at a first operation and found at reoperation. It is noteworthy to point out that all of the cases of multiple primary carcinomas of the small intestine were either found at operation or at autopsy.

The incidence of multiple carcinomata of the small bowel has been discussed by Groff (8), Medinger (12), Mayo (11), Slaughter (16), and others. In eighty cases of carcinoma of the small intestine Groff (8) found one case of multiple carcinoma involving the small bowel alone or an incidence of 1.25 per cent. In two other cases, the first involved the ileum and sigmoid, the second involved the duodenum and stomach. Medinger (12) in a study of 1,456 autopsies and 41,000 surgical specimens found sixteen cases of carcinoma of the small bowel and among these were two multiple carcinomas. The sites of his cases were not stated precisely, whether they were multiple in the small intestine or whether one growth was located in the small bowel and the other elsewhere in the gastrointestinal tract. The incidence of two multiple carcinomas (sites not stated) among sixteen cases of carcinoma of the small bowel (12.5 per cent) seems to be unusually high. Mayo (11) in his study of 104 cases of carcinoma of the small intestine found four with multiple growths (sites not mentioned), an incidence of 3.7 per cent. Slaughter (16) reviewed the literature on multiple carcinomas, found 145 cases of multiple cancers of the gastrointestinal tract, the vast majority of which involved the stomach and colon. Of the multiple carcinomas involving one organ there were four cases in the small bowel; three in the ileum and one in the duodenum. There were ten cases with one growth in the small intestine and the other growths elsewhere in the gastrointestinal tract, namely, four cases involved the small bowel and colon, two involved the esophagus and small bowel, two the jejunum and tongue, one the ileum and appendix, one the duodenum and tongue.

In the present review there were six cases of multiple carcinomata recorded which were limited to the small intestine and nine cases with one growth in the small bowel and another elsewhere in the gastrointestinal tract. Of the six cases, two involved the jejunum and one the ileum; in two the duodenum and jejunum were involved, and in one case the growths were scattered in the small intestine. It is of interest to point out that of the six cases of multiple carcinomas of the small intestine three were reported from the Mayo Clinic by Groff (8) and Judd (9). It is possible that one of the cases recorded may be duplicated by these authors. There are probably an undetermined number of cases, though not many, reported in the literature which were not found nor available in this survey.

Of the nine cases with one growth in the small bowel, the other located elsewhere in the gastrointestinal tract, there were two involving the duodenum and stomach, one the duodenum and sigmoid, one the jejunum and stomach, one the ileum and cecum, one the ileum and sigmoid, one the ileum and rectum, one the ileum and cecum and sigmoid, one the small bowel (site not mentioned) and the esophagus.

Multiple carcinomas of the small intestine may occur synchronously or asynchronously. Of the six cases recorded in the literature all were found to occur synchronously. Asynchronous growths are more common-

*These data were obtained from the autopsy records of the Sinai Hospital through the courtesy of Dr. Tobias Weinberg, Director of Laboratories.

Submitted July 5, 1952.

TABLE I

ANALYSIS OF RECORDED CASES OF MULTIPLE CARCINOMA OF THE SMALL INTESTINE

Author	Autopsies	Surgical specimens	Cases of multiple ca. small bowel	Cancer small bowel and cancer elsewhere	Esophagus	Site Small Bowel Carcinomas: Stomach	Duodenum	Jejunum	Ileum	Small bowel site not stated	Cases Small Bowel CA. with CA. elsewhere in Gastrointestinal Tract: Esophagus	Stomach	Colon	Sigmoid	Rectum	Cecum	Cases of carcinoma of small intestine	Multiple cancers site not mentioned	Per Cent
Bailey (1)			1					++											
Groff (8)			1				+	+									80		3.75
				1					+					+					
				1			+					+							
Bakke (2)			1						++										
Judd (9)		24	1				+	+											8.3
			1							+									
				1					+							+			
Morel & Bolo (13)				1						+	+								
Lorenz (10)				1			+							+					
Medinger (12)	1,456	41,000															16	2	12.5
Mayo (11)				1				+				+					104	4	3.7
Emmet & Dreyfuss (6)				1					+					+					
Daland (5)				1					+						++				
Bunting (3)				1					+					+		+			
Wood & Penna (17)			1					++		+									
Total Cases			6	9															

ly observed in the colon than elsewhere in the gastrointestinal tract.

The clinical diagnosis of multiple carcinomas of the small intestine is often difficult to make. The roentgenologic diagnosis although not impossible would likewise be difficult, since most cases are of the constricting type and therefore obstruct the bowel early, whereas a second lesion at some distant point would be difficult to demonstrate. In the cases recorded the diagnosis was made at operation or at autopsy examination.

COMMENTS

Since the incidence of carcinoma of the small intestine is unusually low, and the occurrence of multiple carcinomas is extremely rare, it might be of interest to conjecture why carcinoma does not attack the small bowel similarly as it does other organs of the gastrointestinal tract. Many theories have been advanced and a variety of reasons can be deduced concerning the comparative rarity of primary carcinoma and multiple carcinomas of the small intestine. Although it is claimed that the fluid content of the small intestine and its rapid transit through the gut militates against the formation of carcinoma, nevertheless the absence of stagnation might be only one of the factors in the etiology of this condition but is probably not the sole cause. Other factors, such as irritation, alkalinity of the small bowel content, absence of abrupt bends in the small intestine have been mentioned as possible conditions which might favorably influence the development of carcinoma. Moreover, it seems that the conditions mentioned would be untenable to consider as factors in counteracting the formation of malignant growths. On the other hand, the possibility of some intrinsic factor such as chemical or hormonal secretion of the mucosa of the small intestine should be given serious consideration. In the light of recent progress on the effect of hormones on malignant growths it is interesting to speculate on the hormonal theory as a plausible etiologic factor in the development of carcinoma of the small intestine. For this reason it seems worthy to comment on the premises of the assumption of the concept that there may be an anticarcinogenetic hormone secreted by the mucosa of the small intestine which might have a deterrent influence in the development of carcinoma or inhibit or counteract the formation of new growth. It is conceivable, however, that suppression of some chemical or hormonal activity of the mucosa of the small bowel may be an important factor in the complex nature of the etiology of carcinoma in this segment of the digestive tract.

CONCLUSIONS

(1) A survey of the available literature revealed an extremely low incidence of multiple primary carcinomata of the small intestine.

(2) Six cases of multiple primary carcinoma were found in which the growths were limited to the small bowel.

(3) Nine other recorded cases were found in which there were multiple carcinomata in which one growth involved the small bowel, the second growth involved other organs of the gastrointestinal tract.

(4) A comment on the etiologic factors rendering the small intestinal segment unfavorable for the development of carcinoma is discussed.

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SUBACUTE ALCOHOLIC CIRRHOSIS WITH HEMORRHAGE FROM ESOPHAGEAL VARICES WITH REFERENCE TO PORTAL HYPERTENSION, AND THERAPY

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THE ADVENT of hemorrhage in patients with early cirrhosis is an unpredictable and frequently lethal complication. Under the guise of supportive therapy designed to correct anemia certain physiological alterations specifically related to portal hypertension tend to augment the pre-existing hemorrhage thus adversely affecting the patient's prognosis.

Complex physiological alterations occur in these patients. To mention a few—portal hypertension, abnormal clotting, reversal of the plasma albumin-globulin fractions, with accompanying edema, and susceptibility of the dilated submucosal veins to erosion by the digestive juices. It has impressed the author that hemorrhage from esophageal varices is analogous to, though not necessarily quite so therapeutically effective as, venous phlebotomy performed for acute congestive failure.

The records of a group of patients whose diagnosis was confirmed by autopsy were studied in order to examine the factors which control massive hemorrhage and to illustrate the problems concerning certain aspects of treatment. The selection of material was restricted to the records of those dying with fatty livers. All these patients had subacute alcoholic cirrhosis. From the clinical point of view, these patients were alcoholics of many years' duration and in this locale such persons are apt to be fortified wine drinkers, undoubtedly because of the comparative lower cost; thus their period of alcoholism may be prolonged. In addition, the sugar content of wines contributes to the suppression of the appetite for natural foods and sustains them through longer periods of malnutrition and probably induces rapid increase in the fatty content of their livers. These patients are subject to hepatic insufficiency, most commonly exhibited by jaundice and ascites, but hemorrhage is by no means unusual.

In Kiefer's (1) group of 51 clinical cases of fatty liver, six died as a result of esophageal hemorrhage. In the series reported by Hall and Morgan (2), consisting of 68 cases selected from autopsy material, the incidence of jaundice was 50 per cent, ascites 63 per cent, and gross esophageal hemorrhage 35.3 per cent. In a recent unpublished postmortem survey of cirrhosis cases selected from the Los Angeles County Hospital, Hall and Davis found the incidence of hemorrhage causing death in 257 patients having subacute cirrhosis to be 10.1 per cent, while in 111 cases of advanced, or atrophic Laennec's cirrhosis, 24 deaths occurred from gross hemorrhage, or 21.6 per cent.

Subacute alcoholic cirrhosis is pathologically characterized as follows: The liver weighs from 2000 Gm. to 5000 Gm., its surface is smooth or granular, usually with diffuse fatty infiltration. The degree of fibrosis is less than in the more advanced cases and various degrees of necrosis are present, accompanied by infiltration by polymorphonuclear leukocytes and lymphocytes.

Fibrosis is not the dominant factor in the inception of hepatic failure (3), although it is an important factor in the chronic cirrhotic liver. The extent of intralobular inflammatory reaction, fatty metamorphosis and necrosis provides a basis for an estimation of hepatic functional impairment. Contrariwise, a clinical appraisal supported by differentiating functional tests indicates the patient's prognosis, but there is by no means a good correlation between functional tests and

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Submitted July 14, 1952.

histopathological findings. Constriction by fibrous tissue, causing distortion and occlusion of the hepatic sinusoids and portal veins, has for many years been considered the mechanism responsible for portal hypertension, except perhaps in isolated cases of portal-vein thrombosis. As a result of repeated injury, necrotic parenchymal cells are believed to be replaced by fibrous tissue. McIndoe (4) elaborated on this theme by demonstrating an obliteration of the hepatic vascular ramifications by injection technique. Kelty (5), however, maintains that there is an unsatisfactory correlation between the degree of fibrous tissue and evidence of increased portal pressure, as substantiated by extensive collateral circulation, esophageal varices, and ascites. He proposed that the proliferating intralobular stroma forms a new framework which compresses and alters the course of the perilobular veins. Elias (6), who re-examined the structure of the liver by both stereographic and injection techniques, demonstrated that the lobular sinusoids, instead of passing along cords of parenchymal cells in a tubular fashion, are more correctly described as intermingling with the parenchymal cells in a saccular manner.

The liver cells are better described as forming laminae, one cell in thickness, adjacent to sinusoidal spaces, which not only course parallel to the parenchymal cells, but perforate in many places the laminae hepatis. This variegated intercommunication of sinusoids, cribriform in character, increases the blood storage capacity of the liver. The sinusoids are irregular, or fusiform, in shape, their width estimated to be from one to six erythrocyte diameters. The hepatic sinusoids do not appear able to change their caliber except passively (7). Changes in size of the parenchymal cell due to either intracellular or extracellular physiological alterations will directly affect the patency of the adjoining sinusoidal lumina. Connor (8) states that the liver may be so engorged with fat that it is enlarged and tense, with sinusoids and central veins collapsed, with degeneration of the swollen cells. Experimentally, employing carbon tetrachloride as a toxic agent upon rats, Himsworth (9) noted that within two to four hours the parenchymal cells throughout the lobule were swollen to such an extent as almost to obliterate the liver sinusoids, preceding by approximately eight hours actual central necrosis. Weser et al (10) conclude that impairment of intrahepatic blood flow seems to be caused by early swelling of the parenchymal cells in carbon tetrachloride poisoning. The avascularity due to occlusion of the sinusoids in very fatty livers of African pellagrins, according to Gillman (11), makes biopsy a safe procedure. Microscopic sections in these

TABLE

Case	Age Sex	Hemorrhage Prior to Admission	Time in Hospital	Ascites or Jaundice	Spleen Weight	Liver Weight	Liver Surface	Microscopic Findings
1	52 M	3 days	2 days	As—0 Ja—0	110 Gm.	2620 Gm.	Smooth	Fat 3+ *C.T. 2+ and infiltrated leucocytes, minimal cirrhosis
2	47 F	1 day	2 days	As—0	190 Gm.	2780 Gm.	Granular	Fat 3+ C.T. 2+ Necrosis 1+ Hyperplasia 3+
3	46 F	3 months	4 days	As—2000 cc Ja—3+ (I.I. 92)**	160 Gm.	2400 Gm.	Granular	Fat 3+ C.T. 3+ Necrosis 3+ Hyperplasia 1+
4	32 F	2 days	2 days	As—100 cc Ja—1+	630 Gm.	3700 Gm.	Granular	Fat 3+ C.T. 1+ Necrosis 2+ Hyperplasia 1+
5	46 M	0	6 days Hem. 1 day	As—500 cc Ja—?	250 Gm.	2270 Gm.	Smooth	Fat 4+ C.T. 2+ Necrosis 3+ Hyperplasia 2+
6	53 M	0	25 days Hem. 2 day	As—1+ Ja—3+ (I.I. 68)	220 Gm.	2950 Gm.	Smooth	Fat 2+ C.T. 2+ Necrosis 3+ Hyperplasia 3+
7	40 M	2 days	1 day	As—0 Ja—0	110 Gm.	3130 Gm.	Smooth	Fat 4+ C.T. 1+ Necrosis 1+
8	43 M	1 day	1 day	As—? Ja—1+	160 Gm.–	2460 Gm.	Granular	Fat 4+ C.T. 1+ Necrosis 1+ Hyperplasia ±
9	29 M	2 days	1 day	As—1+ Ja—0	160 Gm.	2700 Gm.	Smooth	Fat 2+ C.T. 1+ Necrosis ± Hyperplasia 1+
10	37 M	delirium tremens	12 days Hem. 1 day	As—2+ Ja—4+ (I.I. 204)	325 Gm.	3500 Gm.	Granular	Fat 2+ C.T. 2+ Necrosis 0 Hyperplasia 2+
11	40 M	1 day	2 days	As—1+ Ja—1+	300 Gm.	2600 Gm.	Granular	Fat 4+ C.T. 2+ Necrosis 2+ Hyperplasia 2+
12	46 M	0	23 days Hem. 15 day	As—0 Ja—0	275 Gm.	2550 Gm.	Granular	Fat 3+ C.T. 2+ Necrosis 1+ Hyperplasia 3+
13	44 M	3 days	1 day	As—0 Ja—0	550 Gm.	2100 Gm.	Granular	Fat 3+ C.T. 3+ Necrosis ? Hyperplasia 2+
14	55 M	2 weeks	1 day	As—1+ Ja—?	410 Gm.	4570 Gm.	Granular	Fat 3+ C.T. 3+ Necrosis ± Hyperplasia ?
15	40 M	1 day	1 day	As—450 cc Ja—?	370 Gm.	3025 Gm.	Granular	Fat 2+ C.T. 2+ Necrosis 0 Hyperplasia 2+

*Connective Tissue **Icteric Index

instances reveal necrosis as well as considerable infiltration of hepatic cells. Signs of decompensated portal cirrhosis are clinically absent. (See Table).

Clinical Material: The specifications for the selection of cases for study were as follows: 1) Massive gastrointestinal hemorrhage due to verified rupture of esophageal varices as the primary cause of death; 2) A fatty liver weighing over 2000 Gm.; 3) A histopathological diagnosis of subacute alcoholic cirrhosis.

There were 15 cases. The ages of the group varied from 29 to 55 years. Nine died in their fourth decade. (The cirrhotic patient with an atrophic liver usually succumbs in a later decade.) There were three females. Only one patient was not an alcoholic at the time of admission to the hospital. He stated that he had drunk little alcohol for the past 10 years and none since the onset of anorexia, nausea and emesis three years before. For the remainder, the average alcoholic consumption admitted by the patients was about one pint of whiskey or wine (or a combination of the two) each day for a period of 10 to 15 years. More important was the prevalence of severe alcoholism accompanied by anorexia for food for from two or three weeks prior to the onset of fatal hemorrhage.

The existence of portal hypertension is indicated by the presence of esophageal varices, splenomegaly, and ascites shown either on physical examination or proved at autopsy. Jaundice was present in five, and gross ascites determined in nine patients. Four had onset of hemorrhage after admission to the hospital. Ten were admitted within three days after bleeding had become apparent, and 12 died within five days after onset of hemorrhage. (See Table).

The heaviest liver weighed 4570 Gm. and the lightest was 2100 Gm. The surfaces were described as smooth in five cases and granular in the remaining ten. The spleens weighed from 110 Gm. to 630 Gm., with no correlation as to size, surface and degree of connective tissue of corresponding livers. The histologic findings showed moderate to extreme amounts of fat within the hepatic lobules. There was increased perilobular connective tissue of varying degrees. Necrosis of the parenchymal cells was not uniformly present, nor was hyperplasia. As would be expected, there was only a moderate degree of liver cell hyperplasia or regeneration in patients dying in the early subacute stages of cirrhosis. If patients remain in the hospital under treatment for several weeks, regeneration is likely to be much greater (see Cases No. 6 and No. 12 in Table).

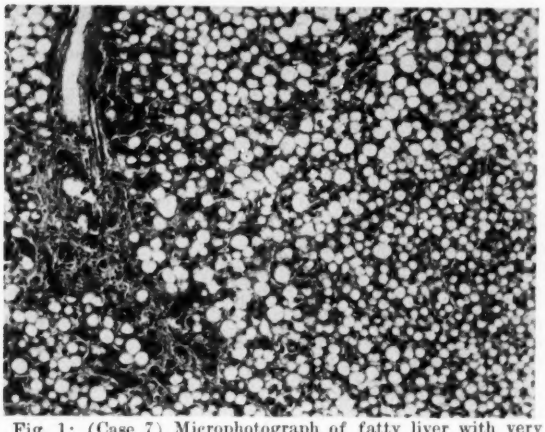

Fig. 1: (Case 7) Microphotograph of fatty liver with very early cirrhosis. Note early cellular fibrosis in portal area, slight intralobular fibrosis and extreme fatty infiltration, with collapse of the sinusoids. Weight of liver 3130 Gm. X 100

Of most significance from a clinical-pathological standpoint is the obliteration, or marked alteration, of the vascular sinusoidal channels from the periphery of the hepatic triad to the central vein. In keeping with the state of shock, many of the sinusoids are congested with blood cells, but over large areas of many lobules no sinusoids are discernible (Fig. 1, 2, 3). There is

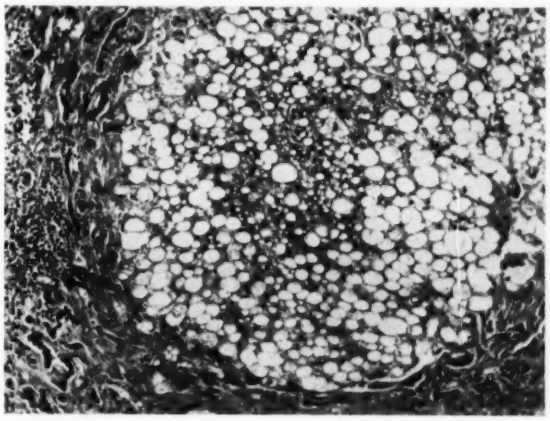

Fig. 2. (Case 8) Microphotograph of liver in subacute alcoholic cirrhosis. It shows portal and perilobular fibrosis and extreme fatty infiltration of the liver cells with obliteration of the blood sinusoids. Weight of liver 2460 Gm. X 100

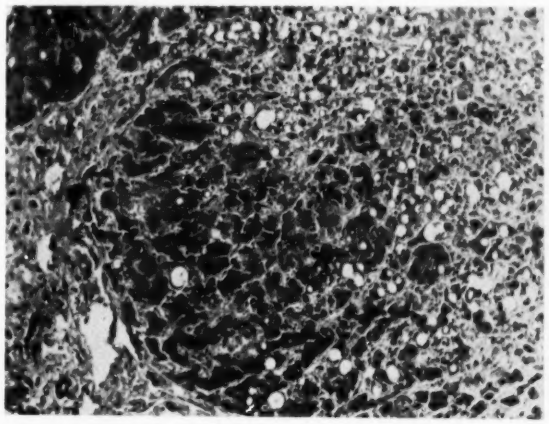

Fig. 3 (Case 6) Microphotograph of liver in subacute alcoholic cirrhosis. There is portal and intralobular fibrosis with only moderate fatty infiltration. The liver cells appear swollen, thus obliterating the sinusoids. Weight of liver 2950 Gm. X 100

decided contrast in sections of the liver taken from patients who died from gastrointestinal hemorrhage due to peptic ulcer compared to those with liver cirrhosis, upon whom the same general principles of medical therapy are used (Fig. 4). It is only after the period of shock has persisted up to 24 hours that central lobular liver necrosis due to anoxia is commonly found, irrespective of the disease suffered (12). The histologi-

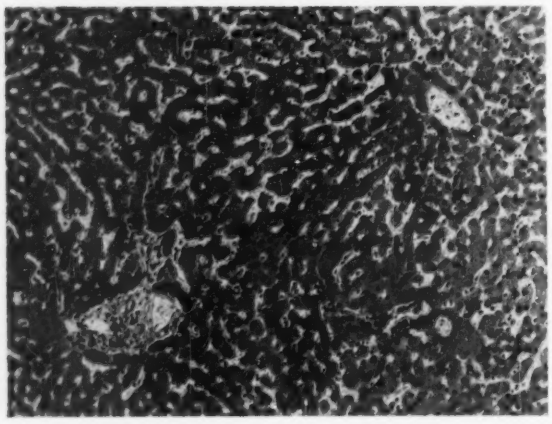

Fig. 4. Microphotograph of liver in patient dying of exsanguination in peptic ulcer. There is normal trabecular arrangement, with widely patent sinusoids, in spite of considerable cloudy swelling of liver cells. No central necrosis is evident. X 100

cal architecture of the lobule is orderly in shock and the sinusoids are ample for blood emptying into the central vein.

In two of 19 unpublished cases of hemorrhage, the precipitating events causing rupture of varices were as follows: The first, a male aged 56, who had a history of alcoholism, had been observed in a hospital for a period of four months for advanced cirrhosis complicated by ascites and jaundice. The patient improved and in May of 1949, prior to his discharge, varices were detected by means of a barium examination. He continued in fair condition until August 31, 1949, when he lifted a crate, and abdominal pain suddenly occurred, followed by persistent discomfort. He was readmitted to the hospital on September 1, because of melena and hematemesis, and died two days later. Autopsy showed a granular liver and rupture of a large esophageal varix. The second patient, a male aged 64, had suffered one hemorrhage and a period of ascites within the previous two years. He was readmitted to the hospital because of melena which had begun after he had loaded watermelons on a truck the previous day. In these cases, the increased intra-abdominal pressure; fixation of the diaphragm, and strain resulted, it would seem, in abrupt elevation in portal-vein tension, with resultant hemorrhage (13).

DISCUSSION

One clinical feature differentiating between the fatty and advanced type of cirrhosis is the rapid response to therapy of the former, following hospitalization. The mortality is high unless a degree of stabilization of the disease occurs. Some of the factors influencing stabilization are the recession of edema within the lobule, improved hepatic circulation accompanying rest, and adequate nutrition for the surviving parenchymal cells. The development of portal collateral circulation to accommodate fluctuating phases of the intrahepatic circulation, in either acute or subacute hepatic injury, requires an interval of time, and this time lag augments portal hypertension and predisposes to hemorrhage. The diminution of portal blood flow does not necessarily parallel the stage of hepatic disease. Dock (14) observed his lowest perfusion rate in a liver weighing 3820 Gm. from an acute alcoholic patient in whom cirrhosis had not yet developed. However, it is apparent that there is a reduction of the entire vascular bed.

Although laboratory animals, given selected diets, are known to acquire fatty infiltration of the liver, yet all the factors necessary to produce this condition in man are less well understood. Alcoholism is a common bond in this series of patients. Alcoholism associated with food deprivation for two or more weeks might well accelerate fatty infiltration upon a pre-existing hepatomegaly. Rats kept on a high-fat diet, when dehydrated, retain a higher percentage of water than do those on a normal diet (15). A tabulation presented by Labby and Hoagland (16) of the fluid shifts in 14 cases of infectious hepatitis during the acute phase of the disease showed average increases of 13.5 per cent increase of the thiocyanate space, 23.4 per cent increase in plasma volume and 27.1 per cent increase of blood volume, as compared with the convalescent phase of the disease.

Susceptibility to marked fluctuations in body water metabolism in cirrhosis may jeopardize the patient in case of zealous, but injudicious, therapy. For instance, Wiggers and his coworkers (17) recorded portal-vein pressures of dogs before, then during arterial hypotension caused by rapid bleeding, and immediately after reinfusion with blood. The arterial pressure was recorded at 50 mm. and at 30 mm. of mercury, and they found that as the arterial pressure declined, so did the portal pressure. However, after reinfusion, portal pressure became elevated far above the control values. Bradley (18) has demonstrated by employing a type of bromsulphalein clearance test that the estimated hepatic blood flow (EHBF) tends to be greatly reduced in cirrhosis. Since there is experimental evidence of marked fluctuation of portal pressure in dogs with normal livers, dependent upon alteration in blood volumes, and evidence of diminished hepatic blood flow in cirrhosis, it seems reasonable to conclude that the portal pressures in cirrhotic patients will be greatly accentuated by a momentary elevated blood volume.

Regarding therapy for the initial hemorrhage and accompanying shock, replenishment of blood and some fluid is essential, but after restitution is made, an excessive amount at any given time will endanger the patient, due to renewal of bleeding. Seavers and Price (19) gave normal dogs transfusions of an average of 275 cc. of blood during a two-hour period, and 30 minutes after termination of the transfusion the blood volume was elevated 123 per cent over the initial blood volume. When the animals were hydrated by stomach tube at the rate of 3 cc. per kilogram per hour, with simultaneous transfusion, there was an abrupt rise in blood volume to slightly over 140 per cent, associated with an eight-fold increased urinary output. A patient having a massive hemorrhage from peptic ulcer, supported by liberal blood replacement and fluids, usually has adequate renal excretion to avoid excessive plasma volume, but one with cirrhosis is handicapped by oliguria. To be more specific, control subjects will excrete 50 percent of 1500 cc. of ingested water in 100 minutes, but the average excretion in cirrhosis of 50 per cent of ingested fluid requires more than 240 minutes (20).

It was determined that normal control subjects would excrete from an infusion of 20 Gm. of sodium chloride at the end of 24 hours a total of 10 Gm. of sodium chloride, while in comparison, the cirrhotic patient averages from 1.2 Gm. to 4 Gm. in 24 hours (21). Goodyer (22) concludes that in all probability sodium is retained by the kidneys as a result of increased tubular reabsorption. This predisposition of the cirrhotic patient to retain both fluids and salts abnormally reflects the vulnerability of the liver to more extensive injury following infusion of isotonic solution of sodium chloride and potassium bicarbonate. It has been shown that the liver of normal dogs has a rather high retention of water, an average of 147 Gm. per kilogram weight of the organ, of which 114 Gm., or 77 per cent, is increase of intracellular fluid (23). This disproportionate increase of intracellular fluid would be reflected by enlargement of the intralobular parenchymal mass at the expense of the intralobular spaces through which course the blood sinusoids and biliary ducts. Selye (24) observed that immediate saline infusion, or bleeding, of 70-per-cent hepatectomized rats would produce marked fatty changes in the liver remnant in 24 hours, while unoperated control rats, similarly treated, showed normal livers. (Swelling of the hepatic parenchyma and anoxemia undoubtedly were responsible for the fatty changes.) The remarkable capacity of the liver to regenerate is reported by Brues et al (25), who examined their 70-per-cent hepatectomized rats and found that 48 hours later the remaining liver fragment had increased 50 per cent in size.

In addition to the need of restraint in the quantities of fluids administered both enterally and parenterally, caution is indicated regarding the means of securing sedation of the patient. It is common knowledge that morphine has a deleterious effect upon the cirrhotic patient. Morphine is detoxified by the liver (26) and in this situation its action is prolonged and the patient may remain stuporous for hours. Morphine, demerol and the barbiturates produce a greatly accentuated antidiuretic effect upon the cirrhotic patient (27, 28, 29).

When a cirrhotic patient is admitted to the hospital with hemorrhage, his acute anemia, degree of dehydration and malnutrition immediately engage the attention of the therapist. Blood transfusion is indicated and should be administered slowly, even in critical cases, in order to guard against unnecessary overloading of the portal system. A rapid infusion, or excessive quantities of blood, will result in a precipitate increase of the blood volume. The portal system, under these circumstances, participates by sharing in the accommodation of these temporary excesses of blood. The citrated solution added to normal blood is probably detrimental to the fatty liver, because sodium causes greater swelling and, in addition, ultimately curtails the volume of renal output. After making allowances for body fluid deficiencies (due to hemorrhage, acidosis, dehydration and other causes), the urinary output must be accounted for. With cirrhosis, even in the absence of hemorrhage, the kidneys can no longer perform their dominant role in adjustment of body fluid metabolism. It is not surprising, therefore, that ascites may form after hemorrhage or that, in spite of best-intentioned replacement therapy, the patient's hemorrhage will continue. Douglas and Snell (30) conclude from their experiments that hemorrhage is the most unpredictable feature of cirrhosis. Usually there is a disturbance of the plasma proteins in these patients and all have, as a result of hemorrhage and malnutrition, depletion of readily-available proteins. These conditions, uncorrected, add to water retention. Particular effort should be made to restore these patients to a positive nitrogen balance, since this sustains them and controls the tendency to chronic shock. A high caloric diet, without liberal amounts of fluids, employed as a vehicle for ingested foods, is desirable; for example, raw eggs, cream, powdered milk, and low-sodium, hydrolyzed proteins are basic foods for continuous feeding.

SUMMARY

In subacute alcoholic cirrhosis, the presence of minimal to moderate amounts of perilobular fibrosis does not preclude a high incidence of fatal hemorrhage from esophageal varices. The gross and histopathological findings in 15 cases of subacute alcoholic cirrhosis are briefly reviewed. All were characterized by livers weighing more than normal and containing moderate to extreme degrees of intralobular fat. Increased connective tissue was present in variable amounts, and necrosis was often present, but hyperplasia was minimal.

More emphasis was directed to the disturbance of intralobular sinusoidal circulation, rather than the concept of a mechanical narrowing, or blocking, of the perilobular portal vessels. The gross structure of the lobular architecture in fatty livers is more like that of a normal liver than that in the more advanced stage of atrophic cirrhosis, but this does not prevent occlusion of its sinuoids, due to extreme fatty metamorphosis of the parenchymal cells.

The role of hemorrhage as a physiological compensatory phenomenon, accompanying rather abrupt deprivation of the intralobular sinusoidal circulation, with a precipitate elevation of portal hypertension, is discussed. It is proposed that caution be exercised during the period of supportive therapy for hemorrhage in patients having fatty livers, to avoid administration of excessive amounts of fluids. This seems necessary because of the disturbed water metabolism, including oliguria, which is present in this disease. Saline solutions, unless there is hyponatremia, not only

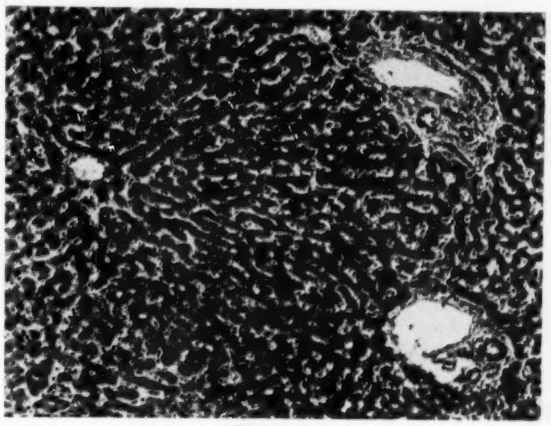

Figure 5.

predispose to oliguria, but are detrimental to the liver parenchyma as well.

Brief mention is made of the fact that not only morphine, but the barbiturates also, act particularly as antidiuretics and in cirrhosis may indirectly, by further impairment of the deranged fluid metabolism, precipitate hemorrhage from esophageal varices.

The author wishes to express his appreciation to Dr. E. F. Hall for his assistance in reviewing the pathological aspects of the paper and for his interpretation of the microscopic sections used.

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SURGICAL CONTRAST VISUALIZATION OF THE PANCREATIC DUCTS WITH A STUDY OF PANCREATIC EXTERNAL SECRETION

LUCIEN LEGER *

THE DIFFICULTIES of clinical and surgical diagnosis of pancreatic diseases, particularly between carcinoma of the pancreas and chronic pancreatitis, have stimulated the study of this problem. Obviously the diagnostic procedures used are of the utmost importance. It appeared to me that emphasis on the need of contrast visualization of the excretory pancreatic channels, particularly the duct of Wirsung, is of capital importance. In view of the lack of adequate means of administering a contrast medium which would reveal, roentgenographically, the pattern of the pancreatic ducts, I suggested in a report issued in collaboration

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with Bréhant at the French Congress of Surgery, held in Paris in 1949, that the pattern of the pancreatic pathways during surgical procedures be made the subject of a careful study.

Studies on the cadaver have convinced my associates and me of the possibility of catheterizing and injecting the duct of Wirsung. The roentgenograms, thus obtained under normal conditions are of a particularly delicate design, and under pathologic conditions they should reveal sufficiently evident changes to give information as to the nature, the exact topography, and the depth and extension of the disease. After duodeno-pancreatic dissection the duodenal papilla is exposed by vertical duodenotomy performed over the second portion of the duodenum. Recognition of Vater's ampulla is facilitated by pressure on the gallbladder. Catheterization of Wirsung's duct is performed with a special polyethylene tube, 1 mm. in diameter. A possible error consists in catheterization of the biliary common duct, but observation of the reflux of bile promptly clarifies the situation. It is particularly noteworthy that pancreatic catheterization causes the flow of a clear liquid anytime with white particles, or, no discharge issues. Thus, the absence of discharge of bile indicates that the proper course is being pursued and the desired effects will result.

Also, the first liquid obtained after introduction of the catheter into Wirsung's duct reveals a golden-yellow reflux, giving the false impression that the catheter has not entered the proper avenue but has found its way instead into the common duct. This is an erroneous impression. Under such conditions one wonders whether, perhaps a little bile has been aspirated by capillarity into the polyethylene tube during its passage across the ampulla; or, does it, perhaps, represent a reflux of bile into the excretory ducts of the pancreas? It is reassuring to note that the stylet, rubber bougie or polyethylene tube passes more easily into Wirsung's duct than into the common bile duct, though one would be inclined to believe the opposite.

Two to 3 cc. of 70 per cent *"diodone"* is now injected into the pancreatic duct, and a roentgenographic exposure is made.

One of the difficulties, and not the least, lies in the fact that with the portable roentgenographic units used at the operating table the exposure time is necessarily prolonged. Although respiration may be suppressed by the anesthetist and the interference of respiratory movements thus eliminated, the transmission of aortic pulsation is likely to cause considerable distortion of the image. This is a common observation in all roentgenograms of the pancreas. To obtain clear images of pancreatic concretions, etc., one should keep in mind the importance of short exposures. The problem,

Fig. 1. Visualization of Wirsung's duct during an operation for cholelithiasis. Normal roentgen appearance. Note extremely oblique course of Wirsung's duct.

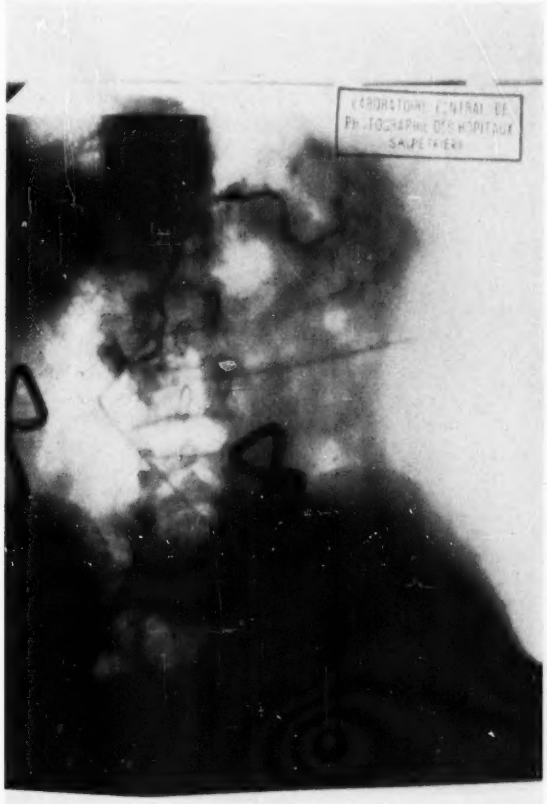

Fig. 2. Stricture of the Wirsung's duct at the pancreatic isthmus. In more than half of our cases, our Roentgenograms have revealed a narrowing of the Wirsung in the segment that crosses the isthmus.

therefore, is to obtain brief exposures that are yet long enough to result in sufficiently dense negatives.

In the absence of sufficiently powerful equipment in the operating room, our exposures have been obtained with a mobile unit by simply bringing the tube as close to the patient as possible. We place the tube at a distance of 20 cm. from the abdominal wall, which permits us to reduce the exposure time to 0.3, 0.4 or 0.5 of a second.

It is possible that this technique results in slight distortion of the peripheral area of the picture; this, however, is not too disturbing. The method also causes a certain enlargement of the image, which may be rather advantageous. The use of a grid is in no way harmful; we always use it.

The reproductions here presented give an idea of the results that may be obtained by our procedure; the duct of Wirsung, the avenues of its origin and sometimes the acini of the pancreas are injected perfectly.

We leave the polyethylene tube in situ, in Wirsung's duct, whence it is made to emerge through a tiny gap in the wall of the duodenum, which is sutured at two places and attached to the anterior parietal peritoneum. This technic allows us to obtain pure pancreatic juice and to study its chemical characteristics and the function of the gland.

The roentgen examinations described can be repeated several times during the operation, and also on the following days, to verify the position of the polyethylene tube in Wirsung's duct. All of our patients made good recoveries. Scar formation was, in no way, retarded. The surgical procedures are simple.

In no case have these maneuvers been followed by acute abdominal symptoms indicating any untoward occurrence. A word of caution is in order here; namely, that one should limit the amount of contrast medium and inject it under reasonable pressure.

Temporary jaundice may occur, indicating partial obstruction of the papilla or its irritation by the tube left in situ.

Under pathologic conditions, when an obstacle such as a tumor of the head of the pancreas is present and associated with dilatation of Wirsung's duct, it seems feasible to puncture the pancreas with a needle at the level of the isthmus of the body of the pancreas or of Wirsung's duct, to aspirate pancreatic juice under tension, to inject the contrast medium, and to obtain a descending contrast visualization as I have suggested in collaboration with J. Bréhant; thus far, however, we have had no opportunity to verify this. The technic here outlined, which is undoubtedly much simpler than any we have known before, should obviously be re-

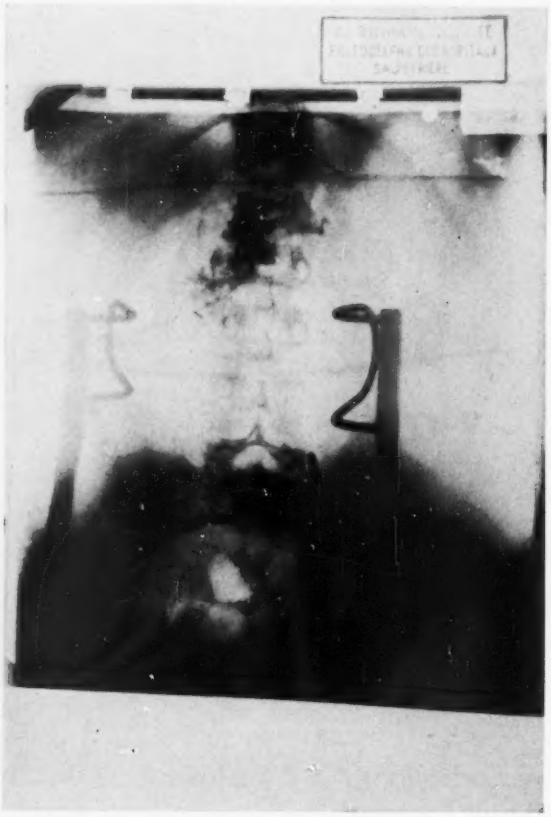

Fig. 3. Visualization of Wirsung's duct during an operation. Note crisp outline of glandular acini of pancreas, which appear dilated. Patient had chronic pancreatitis. Note clip placed at level of papilla in this roentgenogram.

Fig. 4. Visualization of pancreatic ducts during operation for malignant disease of papilla. Observe dilatation of Wirsung's duct and reflux of material to dilated common duct.

served for cases in which there is marked dilatation of the excretory ducts of the pancreas.

A possible criticism of our method of transpapillary catheterization is that it necessitates a duodenotomy; but it remains to be seen whether in any case this procedure does not constitute an advantage.

ROENTGENOLOGICAL ASPECTS

I. *Normal aspect of Wirsung's duct.* Often we note an extremely oblique course of Wirsung's duct (Fig. 1).

II. *Stricture of the Wirsung's duct* at the pancreatic isthmus. In more than half of our cases, our Roentgenograms have revealed a narrowing of the Wirsung in the segment that crosses the isthmus.

This aspect of stricture which exists on two successive radiograms and with progressive distention of the duct, does not seem to be an artefact as the immediately proximate segments of the duct swell out when in contact with the stenosis.

This stricture however, may be perhaps purely functional since it appears only on some of the roentgenograms. On the contrary, it appears typically organic in one case where the enormous dilatation of the Wirsung's duct by an ampullary carcinoma does not prevent the stenosis from being visible.

This stricture in the pancreatic isthmus may be the setting off of a disease, a case of which has just been reported by Appleby (*Archives of Surgery*, vol. 63, No. 1, juillet 1951, p. 115).

The strictly medial position of this stricture is worthy of some more comment.

Dr. Mallet-Guy called attention to the left chronic pancreatitis. This localized aspect of the pathology of an organ striding over the medial line, and the right and left segments of which have a different embryologic formation, should be explained by this medial stenosis of the excretory duct, either organic or functional.

III. *Chronic pancreatitis.*

The aspect of distention of the acini similar to the image that one obtains in cadaveric pancreatography, must be in relation with a dilatation or a lack of normal tonicity of the glandular acini. (Fig. 3).

Our opinion is that it gives evidence of the presence of chronic pancreatitis. We believe moreover that this drainage of the Wirsung's duct is an available therapeutic procedure in chronic pancreatitis as some of our cases proved it.

IV. *Pancreatic carcinoma.*

In a pseudo-aneurysmal form of carcinoma of the pancreatic head which extended in the body, and with-

Fig. 5. Pseudo-carcinomatous chronic pancreatitis. Dilatation of the Wirsung's duct, of collateral ducts and of the acini.

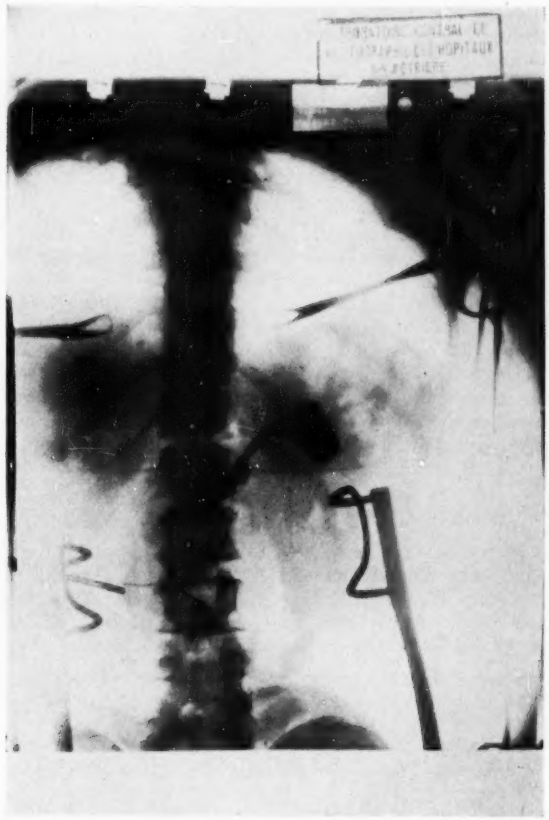

Fig. 6. Pancreatic carcinoma. Considerable dilatation of the Wirsung's duct with irregular outline.

out jaundice, the Wirsung appears on the radiogram with an enormous dilatation irregularly outlined (Fig. 6).

Such an enormous distention of the pancreatic duct, as revealed by pancreatography in carcinoma, explains why Cattell has suggested and performed an anastomosis between the Wirsung and the jejunum in a purely palliative purpose.

The *biological study of pancreatic external secretion* collected in pure condition, allows us to assert that the pancreatic secretion contains *active trypsin*, but no trypsinogen, which goes against the classical opinion, and this even when no intestinal enzyme is present.

These observations allow us to express some reserves as to the classical pathogeny by flowing back in the hemorrhagic acute pancreatitis.

FIVE ECHINOSTOMES FOUND IN MAN IN THE MALAYAN ARCHIPELAGO

C. BONNE, M. D.,† G. BRAS, M. D.* AND LIE KIAN JOE, M. D.

WE RESTUDIED the echinostome material brought together in our laboratory before World War II, supplemented with some new specimens, which one of us had the opportunity to collect at human autopsies during the Japanese occupation and thereafter. We came to the conclusion, that as far as our material from autopsies in humans goes, five species of echinostomes must be recognized. It is our purpose to give in the following pages a short description of these 5 species together with some information about their reservoir-hosts, their lifecycle and their development under experimental conditions in various laboratory animals. We realize the difficulties of echinostome taxonomy as discussed by Beaver (1) in his monograph on Echinostonum revolutum and we share his opinion that the number, the arrangement and further characters of the circumoral spines offer the most dependable criteria for specific differentiation. Although we use the generic names Euparyphium and Echinoparyphium in our descriptions this should not be interpreted to imply that we consider the creation of these genera as fully justified.

Before describing the various species, we wish to remark that conditions of fixation and contraction influence their dimensions considerably. There is also a pronounced liability to disintegration through the action of the host's digestive enzymes. This results in a loss of turgor, abnormal length and flattening of the worms. Living specimens often roll up ventrally and show a reddish tinge of their body, most distinctly present in the area of the uterine coils. This reddish color is not due to the presence of blood in the intestinal canal; it disappears after fixation.

I. *Euparyphium ilocanum* (Garrison 1908)

Garrison (2) discovered this human parasite in the Philippine Islands and gave it the name Fascioletta ilocanum. Odhner (3) recognized the circumoral spines and redescribed it as an echinostome. Tubangui & Pasco (5) worked out the lifecycle.

Euparyphium ilocanum has been repeatedly found in the small intestine of mentally abnormal persons in the island of Java (4) and in a smaller number of cases also in normal individuals. More than 250 specimens have been collected from a single patient. The main reservoir host is the common field rat of the rice fields, Rattus rattus brevicaudatus.

DESCRIPTION OF THE ADULT WORM

(See Plate II, Fig. II)

Length 4-10 mm. Width 0.5-1.5 mm.

Oral and ventral sucker rounded, diameter about 150 μ and 500 μ respectively in fullgrown specimens.

Cuticula with small spines, extending dorsally from the head to the acetabular area and ventrally beyond the acetabulum covering two-thirds of the length of the worm.

Circumoral spines (plate I, fig. 5), implanted on a horse-shoe shaped collar, ventrally open. Total number of spines varying between 50 and 60, usually 51-53. There is a group of 5 spines on each ventral lappet. 3 oral ones and 2 placed more aborally, of which the lateral aboral spine is the largest. This ventral group is followed by 8 pairs of lateral spines on each side and dorsally the row is closed by 11 spines, of which the arrangement is best described as extremely "untidy." The resulting spine-formula is (8+2)+(8+8)+11+(8+8)+(2+3) for a specimen with 53 spines. Very often the first lateral couple of spines loses one spine, resulting in a specimen with 51 spines, the usual number of spines mentioned in the literature for E. ilocanum. The circumoral spines are small, most of the laterals measure 30-45 μ but the medio dorsal spines may be as small as 13 μ. Sometimes it is difficult to distinguish a dwarfed circumoral spine from a large cuticular spine.

Length of pharynx 200 μ, diameter 160 μ.

Genitalia: *Vitellaria* cover one-fifth of the body width on each side and *do not reach the level of the posterior acetabular rim*. Follicles of uniform size; posterior to the testes the follicular fields encroach on the ceca and fuse in the median line over a certain distance. Testes in the posterior half of the body in tandem position, touching the vitellaria with their lateral borders, *rounded or slightly lobed but never deeply incised*. Ovary anterior to the testes and much smaller, rounded, largest diameter about 300 μ. Mehlis' organ irregular in shape. Uterus filled with a large number of eggs, coiling with many loops from the region of the ovary to

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the genital pore situated near the bifurcation of the intestine directly anterior to the acetabulum.

The terminal part of the deferent duct developed into a *cirrus pouch reaching backwards halfway the acetabular opening or beyond.*

Eggs oval, usually yellowish, with small faintly recognizable operculum. Sometimes a trace of thickening of the shell at the opposite pole. In many eggs the nucleus of the ovum is visible. Length 96-111 μ (average 103 μ); width 58-62 μ (average 59.5 μ). These measurements are taken from 20 eggs after fixation in formalin.

Development: First intermediate host Anisus convesiusculus. Second intermediate host Viviparus javanicus, Viviparus rudipellis, Pila conica, Lymnea rubiginosa, Anisus convexiusculus and Contradens contradens (a mussel).

Feeding experiments gave positive results in rats and men. Euparyphium ilocanum has also been obtained in Celebes in experimental infections of rats with Pila conica and Viviparus rudipellis (6).

II. *Echinoparyphium recurvatum* (v. Linstow 1873).

We found this small echinostome several times concurrently with Euparyphium ilocanum in autopsies of patients from a lunatic asylum living together in a rural colony near Batavia. Nearly all of these worms were rolled up ventrally in the shape of the letter C and they usually were less flattened than the accompanying specimens of E. ilocanum. The main reservoir host is the common field rat of the rice fields, Rattus rattus brevicaudatus. We also have specimens from naturally infected fowl.

DESCRIPTION OF THE ADULT WORM

(See Plate II, Fig. I)

Length 2.5-5 mm. Width about 0.4-0.7 mm. Diameter oral sucker about 160 μ acetabulum about 300 μ. The integument is provided with small spines, extending dorsally to the acetabular area and venturally beyond the acetabulum. Most of the worms have lost these spines however.

The number of circumoral spines (plate I, fig. 3) is 45 with very little variation in the total number. They are very large for such a small species, slender and very regular in position. The ventral lappets of the well developed spinebearing collar closely approach and may actually touch each other in the median line. Each of these bears 5 spines, usually 3 oral ones and 2 aboral ones. The lateral aboral one is the largest spine as a rule, but sometimes it shifts its position into the oral row. Next to the 5 corner spines come 2 single spines in the aboral row and all the 31 other lateral and dorsal spines are alternating in position. On the sides of the head, the oral spines are distinctly longer than the aborals but near the median line the aboral spines become larger and may even exceed the oral ones in length. The usual size of the dorsal spines is between 40 and 60 μ, some exceptionally small spines may be not longer than 30 μ. The long corner spines may reach 80 μ in length.

The spine formula is (3+2)+(0+2)+(16+15)+(2+0)+(2+3).

Pharynx, bulbus, esophagus and intestinal ceca are of the usual shape. Length of pharynx 200 μ, diameter 200 μ. Distance between oral sucker and acetabulum 1 mm. for a specimen with a total length of 4 mm.

Vitellaria with their anterior margin *separated from the acetabulum by a considerable distance.* In the middle part of the body they are extra-cecal but they encroach on the ceca and fuse mesially over a small distance posterior to the testes. Uterus filled with eggs with the pore anterior to the *acetabulum. Testes* in tandem position, *without distinct lobes.* The rounded ovary and Mehlis organ anterior to the testes. *Cirrus pouch extending backwards halfway the acetabular opening.*

Eggs oval, yellowish. Nucleus of the ovum not always visible. Dimensions: Length 73-107 μ, width 50-61 μ. Averages for 42 eggs, taken from the uterus in formalin 91.5×57 μ.

Development: First intermediate host Anisus convexiusculus. Second intermediate host Viviparus javanicus, Lymnaea rubiginosa, Anisus convexiusculus, Contradens contradens. Feeding experiments gave positive results in pigeons, rats and a cat.

This parasite comes very near to Euparyphium murinum (7) described in 1931 by Tubangui from the rat in the Philippines. The length of the circumoral spines is given by Tubangui as 35.3-45.7 μ for E. murinum. The species described here has much larger

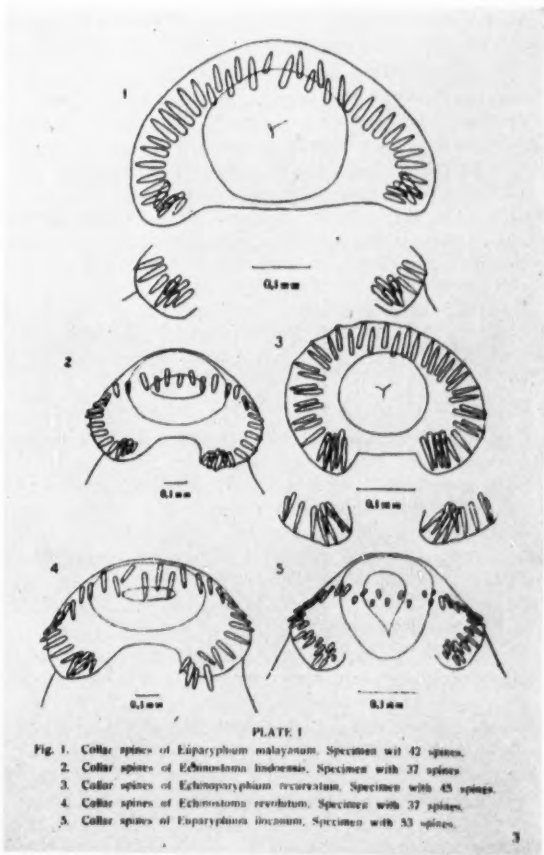

PLATE I

Fig. 1. Collar spines of Euparyphium malayanum. Specimen with 42 spines.
2. Collar spines of Echinostoma lindoensis. Specimen with 37 spines.
3. Collar spines of Echinoparyphium recurvatum. Specimen with 45 spines.
4. Collar spines of Echinostoma revolutum. Specimen with 37 spines.
5. Collar spines of Euparyphium ilocanum. Specimen with 53 spines.

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spines, i.e. ranging from 30-80 μ and most of them with a length of 40-60 μ which coincides better with E. rucurvatum, reported by Tubangui from ducks in the Philippines (8). There remains some doubt with regard to its exact lasonomical position.

III. *Euparyphium malayanum* (Leiper 1911).

Leiper (9) described this fluke in 1911 as Echinostoma malayanum. His material came from the intestine of Tamils in Singapore and Kuala Lumpur. It was redescribed by Odhner in 1913 (10). Both descriptions mention as a characteristic the great width of the worm, the large size of the cirruspouch and the deeply incised testes.

In the Malayan Archipelago E. malayanum has only been met with in Northern Sumatra. In a postmortem of a 12 year old Batak girl 750 specimens were recovered. There is no certainty yet about the reservoir host.

DESCRIPTION OF THE ADULT WORM

(See Plate II, Fig. III)

Length 5-9 mm., width 2.2-3 mm. These measurements were taken from specimens in formalin. Body curved ventrad. It is the broadest of all human echinostomes species in our collection.

Diameter oral sucker about 300 μ, acetabulum 800-1000 μ.

Cuticula with small spines all over the ventral surface and extending on the dorsal surface to the level of the acetabulum.

Circumoral spine-bearing collar, (see plate I, fig. 1) horse-shoe shaped, open ventrally. Number of spines 41-45, without pronounced variations in length, usually 50-70 μ. The ventral lappets bear 6 spines each, followed by 10 lateral spines for a specimen with 43 spines. One spine which falls out of line with the 10 lateral spines because of its more aboral position, and hence increases the usual number of five spines on the lappets to six. Of the 10 lateral spines, No. 6, 7, 8 and 9, counting from the lappet, are larger than the aboral ones in the median area, more laterally the aboral ones are a little larger. Spine formula (3+3)+(0+10)+(6+5)+(10+0)+(3+3).

Length of pharynx about 300 μ, diameter 250 μ.

Vitellaria with their anterior margin *at the level of the acetabulum*. Posterior to the testes they fuse in the median line over a short distance. Follicles uniform in size. *Testes* extending into anterior half of the body, *very deeply and broadly incised*. Ovary anterior to the testes, oval, its largest diameter transverse, about 400 μ. Uterus filled with large numbers of eggs. *Cirruspouch* usually not clearly visible, but *extending beyond the acetabulum when distinct*.

Eggs, oval, yellowish, large, operculated, often with a little knob opposite the operculum. Nucleus of the ovum visible. Dimensions 130-149 μ×70.5-84 μ. Averages 137×75.5 μ for 40 eggs from the uterus of worms after formalin fixation.

Leiper originally described 42 spines for this species, Odhner counted 43 spines, the number usually mentioned in the literature. We counted 41-45 spines but we have no objection to consider 43 the normal number of circumoral spines for E. malayanum. Artyfechinostomum surfartyfex described by Lane (11) in 1915 from Assam seems to be closely related but has definitely smaller eggs, 39-42 circumoral spines and other peculiarities and is better kept apart.

Development: No details about the life cycle of this species from the island of Sumatra are known to us.

IV. *Echinostoma revolutum* (Froelich, 1802)

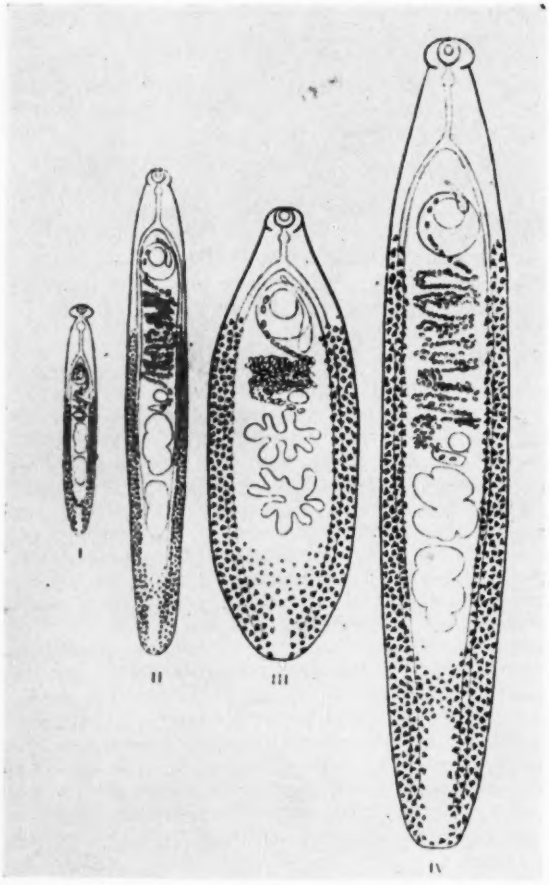
This fluke is normally a parasite of birds e.g. ducks, fowl, small mammals. It has almost a world wide distribution and in Java we have seen it several times in ducks, fowl and also in rats. Two times in Batavia a single specimen was found in post mortems on Indonesians, in one of the two cases the patient was mentally deficient. In a third patient, an Indonesian boy of about 8 years, not less than 85 specimens were discovered together with about 10 specimens of E. ilocanum, and a number of hookworms and Trichuris.

DESCRIPTION OF THE ADULT WORM

(See Plate II, Fig. IV).

Length 10-14 mm. Width 2-3 mm.

Diameter oral sucker 400-450 μ; acetabulum about 1 mm. Cuticula with small spines extending dorsally to the level of the acetabulum and ventrally to the level of the ovary.



Reprinted from Medical Maandblad, June 1948. Plate II.

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The horse-shoe shaped circumoral collar has 37 spines (see Plate I, Fig. 4). The ventral lappets bear 5 spines, followed by 6 lateral spines in a single aboral row and 15 alternating dorsal spines. On the lappets the lateral aboral spine is the largest: length very often more than 120 μ and the median oral spine the smallest. The lateral spines measure 95-123 μ, the dorsal ones 100-125 μ.

The spine formula is (3+2)+(0+6)+(8+7)+(6+0)+(2+3).

Length of pharynx 280-370 μ, diameter 260-290 μ.

Vitellaria extending *from the posterior rim of the acetabulum* to the posterior end of the body, encroaching on the ceca and fusing over a short distance in the median line posterior to the testes. Follicles of uniform size. *Testes* in posterior half of the body, near each other in tandem position, *slightly lobed*. Ovarium halfway the length of the body, oval, its largest diameter, transverse, measuring about 400 μ. Mehlis organ clearly visible. Uterus with about 12 coils containing hundreds of eggs. *Cirruspouch* small, *hardly reaching the anterior rim of the acetabulum*.

Eggs yellowish, oval, operculated. Dimensions: 108-116 μ×52-56 μ for 10 eggs after fixation in formalin. Nucleus of the ovum visible.

Development: First intermediate host Lymnaea rubiginosa, Anisus convexiusculus. Second intermediate host Viviparus javanicus, Pila conica, Lymnaea rubiginosa, Anisus convexiusculus, Corbicula rivalis (a mussel) and other Corbicula species of uncertain taxonomic position.

Feeding experiments gave positive results in pigeons and white rats.

The morphology of the adult corresponds well with the description of E. revolutum by Beaver and we find no differences with the 37 spined echinostomes from ducks, fowl and field rats (Rattus rattus brevicaudatus) in Java. Obviously this parasite has no distinct host-specificity.

V. *Echinostoma lindoensis* (Sandground & Bonne 1940)

Sandground and Bonne (12) described this parasite from a heavily infected primitive tribe of Toradja's living on the shores of Lindoe Lake in Central Celebes.

DESCRIPTION OF THE ADULT WORM

It is a large echinostome like E. revolutum, which it resembles so much, that we use the same Fig. IV of Plate II for the general morphology of both species. It also has the same total number of spines, 37, and the same spine formula (3+2)+(0+6)+(8+7)+(6+0)+(2+3), with the lateral aboral spine the biggest of the five ventral lappet spines and the median oral one the smallest. The shape and the size of the spines differ however, in E. lindoensis they are less slender and they are shorter. Sandground and Bonne give 95 μ as the size of the largest spine seen on any of their specimens studied. In exceptional cases we found a still greater length for the largest lappet spine, in one case even 120 μ in fullgrown specimens. It was very often more than 120 μ in our specimens of revolutum from Java. In the lateral and dorsal series the largest spine ever observed by us in E. lindoensis was 102 μ, their usual length being 60-90 μ. In the specimens of E. revolutum from man in Java the visible dorsal and lateral spines range from 95-125 μ, nearly all of them being more than 100 μ. (See Plate I, Fig. 2). Length of the body 13-15 mm., width 2-2.5 mm. Diameter oral sucker 230-500 μ; acetabulum 600-1300 μ. Cuticular spines extending to the level of the posterior testes. *Vitellaria* extending *from the posterior rim of the acetabulum* to the tail end of the body. *Testes* in posterior half, *lobed but the incisions not exceeding half of the diameter of the testis in depth*. Ovary oval, with the largest diameter transverse, halfway the length of the body or slightly postequatorial. Uterus with about a dozen loops with many hundreds of eggs. *Cirruspouch hardly reaching the anterior rim of the acetabulum*. Eggs yellowish, oval, operculated.

Dimensions: 91.5-107×65-72.5 μ. Averages for 40 eggs from the uterus in formalin 101×69 μ. Nucleus of the ovum always visible.

Development: First intermediate host *Anisus sarasinorum*. Second intermediate host *Viviparus rudipellis, Corbicula lindoensis*, a mussel.

Feeding experiments gave positive results in rats and man and in a few cases in pigeons and young ducks. In old ducks and fowl no infections have been obtained.

Corbicula lindoensis is an important article in the diet of the inhabitants of the Lake Lindoe villages, which explains the almost general infection present in some of them. Steaming or boiling of these mussels is incompletely done in a very primitive way.

Sandground & Bonne (12) noticed the absence of E. lindoensis in the wild ducks and other waterbirds of the lake, which are plentiful and in the chickens of the villages. This made the identity with E. revolutum very doubtful. Experimental infections by Bonne (13) with ducks and pigeons gave poor results. Experimental infections in man, on the other hand, were always successful and produced large numbers of adult worms (12) (13).

After reconsidering the minor morphological differences between E. lindoensis and E. revolutum enumerated by Sandground & Bonne and restudying the material now at hand, we are inclined to attach most importance to the differences in size and shape of the collar spines. The collar spines of E. revolutum are longer and more slender than those of E. lindoensis.

DISCUSSION

It is only by the ingestion of metacercariae-carrying molluscs that man gets infected with echinostomes. Snails and mussels do not rank high however in the culinary estimations of the Indonesians and regular consumption of these molluscs is only met with in the poorer districts. As far as we know it is not a habit to eat them raw and the possibilities of infection depend on the chances for the molluscs to escape sufficient heating in the cooking process, which is not always very thorough. For insane individuals, walking around in the villages or brought together in rural colonies who pick up and swallow anything which looks edible, the risks of infection are especially great and this explains why the incidence of echinostomiasis is so high amongst them as compared with the usually sporadic infections in the general population.

E. ilocanum is probably a very widely spread species in the Far East. Originally described from the Philippines it proved to be very common in Java and we also have it from the Celebes. Its natural host is the rat and human infections are only incidental.

E. recurvatum accompanies E. ilocanum occasionally in human infections. Its reservoir hosts are rats but also birds, fowl and ducks. In man it has only been discovered in Java but obviously as in E. ilocanum man does not count amongst the essential hosts. E. murium is a closely related species with 45 collar spines reported from rats in the Philippines by Tubangui, but it does not develop in birds and has smaller collar spines. We have specimens from the Celebes which also do not develop in birds, resembling E. murinum, which we obtained in rats in feeding experiments with Viviparus rudipellis and Corbicula lindoensis. No human infections with E. murium are known to us yet.

E. malayanum is very distinct and easily recognizable because it is such an unusually broad echinostome and further by the number and arrangement of the collar spines. Originally reported from Malaya, it has later been found in Sumatra and India. We have no information about its life-cycle or its reservoir hosts in Sumatra.

E. revolutum is a cosmopolitan parasite of domestic birds. Infections of man have been reported from Japan and in this paper we add some new cases from Java.

E. lindoensis is only known from three small villages at Lake Lindoe in Central Celebes where a large part (up to 96% in one village) of the inhabitants is infected on account of a large scale consumption of Corbicula lindoensis. No reservoir host has been found and in this unique focus human infections seem to play the principal role in the maintaining of the lifecycle of the parasite. Notwithstanding its morphological resemblance with E. revolutum, the biological behaviour of E. lindoensis is entirely different.

A certain number of genera have been created amongst the echinostomes on differential characters which do not look very sound to us. But we leave the taxonomy to the specialists in helminthology. We agree with Beaver that the number, the position and other characters of the collar spines offer a reliable base for specific differentiation. The number of the collar spines is fairly constant for the echinostomes with 37 spines (E. revolutum and E. lindoensis) and 45 spines of (E. recurvatum and E. murinum) where variations are practically limited to one spine plus or minus E. ilocanum with 50-60 spines however has a very wide range of variation in their number. In E. malayanum with 41-45 spines this range is restricted again. But not only the total number of spines is important, also their arrangement, which finds its expression in the spine formula. In closely related species with the same number of spines the relative size of the spines may still be different.

Other important characters are the shape of the testes, which may be round, slightly lobed or deeply lobed. Post mortem changes influence the lobation however. The extension of the vitellaria and the development of the cirruspouch also have distinct diagnostic value.

SUMMARY

Five echinostome species have been found in man in the Malayan Archipelago, with the following names and spine formulas:

Euparyphium Ilocanum. Spine formula (3+2)+(8+8)+11+(8+8)+(2+3).

Echinoparyphium Recurvatum. Spine formula (3+2)+(0+2)+(16+15)+(2+0)+(2+3).

Euparyphium Malayan. Spine formula (3+3)+(0+10)+(6+5)+(10+0)+(3+3).

Echinostoma Revolutum and E. Lindoensis. Spine formula (3+2)+(0+6)+(8+7)+(6+0)+(2+3).

Echinostoma Lindoensis shows special adaptation to man; all the others are only incidental human parasites with reservoir hosts in rats and birds.

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INFLUENCE OF TANNIC, TARTARIC AND OF ACETIC ACID UPON OLFACTORY ACUITY AND SENSATIONS ASSOCIATED WITH FOOD INTAKE. (A NOTE CONCERNING THE APPETITE STIMULATING EFFECT OF WINE.)

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IN RECENT reports (1, 2) from this laboratory evidence was presented to show that in normal individuals meals are preceded by a period of increasing and followed by one of decreasing acuity of olfaction. In discussing these and related observations the suggestion was made that the precibal increase in olfactory acuity may represent a measurable characteristic of sensations constituting the desire for food and that the postcibal decrease in olfactory acuity may represent a measurable characteristic of sensations constituting the satiety afforded by food.

Meanwhile this approach to problems concerning sensations associated with food intake has been employed in investigations regarding the influence upon these sensations of wine constituents and of wine itself. Studies along these lines revealed that ethyl alcohol (3, 4) in amounts contained in wine produces simultaneously a decrease in olfactory acuity and a sensation of satiety. This observation was interpreted to indicate that the assumed ability of wine to create or augment the sensation of appetite may be dependent upon actions of substances other than ethyl alcohol contained in wine. Since ethyl alcohol was noted to depress the sensation of appetite, the suggestion was made, that the substances postulated, in order to create or augment the sensation of appetite, would have to be capable also of counteracting sufficiently the depressant effect of ethyl alcohol. In view of considerations along these lines it appeared desirable to investigate the influences tannic, tartaric and acetic acids—all contained in many food items and in wine—may have upon olfactory acuity and the sensations associated with food intake. The present study was undertaken with this purpose in mind.

METHODS

Olfactory thresholds were determined by means of a method originally described by Elsberg and Levy (5), and described in detail in previous reports from this laboratory. In principle the method consists of injecting variable but measurable volumes of odorous air into both nasal passages of an individual during a period of momentary cessation of breathing, the force of the injection taking the place of ordinary respiratory movements. As the volume injected and its pressure are known, the test is a quantitative one.

The apparatus used for the test includes a bottle containing a constant amount of odorous substance. The bottle is closed by a rubber stopper which contains inlet and outlet tubes. A nosepiece ending in two olives is connected with outlet tube by means of a pure gum rubber tube which is compressed by a pinchcock. The inlet tube is connected with a syringe permitting injection into the bottle of variable though measurable volumes of air. Care is taken to assure air tightness throughout the system.

The procedure consists of injecting a known volume of air into the bottle and of releasing it into the nasal passages of the subject by pressing upon the pinchcock. The smallest volume of air which suffices to produce the sensation of the odor used was interpreted as the measure of threshold for the sense of smell for the subject at the time. At each determination the threshold value accepted for the subject was the smallest volume of odorous air which produced the sensation of the particular odor three times in succession.

The odor used in the present experiment was that of coffee. Ground coffee of a standard brand and in constant amounts was renewed in the bottle regularly once a month.

On test days the subjects were examined with respect to patency of their nasal passages. This was done by having them exhale through their nose upon a metal mirror. On the polished surface of the mirror the spots produced by the vapor from each side of the nose had to be of equal size and fade out at an equal rate. Only when these requirements were fulfilled could the subject participate in the study.

The procedure was fully explained to the subjects. They were instructed to insert the nose piece and hold it in place so as to permit the escaping odorous air to reach the olfactory region of the nose. They were requested to state whether or not they could recognize the odor upon its escape into the nose during the moment of cessation of breathing. Sensations which were experienced at a later moment were disregarded. The subjects had to remove the nosepieces and to breathe restfully for 30 to 60 seconds between successive trials.

The present experiments were performed with the cooperation of 21 men and women ranging in age from 22 to 53 years. They were in apparently good health. They held clerical positions in this institution and worked daily from 9 o'clock in the morning to 5 o'clock in the evening. As a rule they had breakfast and dinner at home but ate lunch in the hospital cafeteria which offered a variety of dishes, permitting reasonably free selection of food. Lunch was served between 12 and 1 o'clock in the afternoon. On test days the subjects' olfactory thresholds were determined at 10:00 and 11:30 in the morning and at 1:00, 3:00 and 4:30 in the afternoon. On these days the subjects' statements regarding sensations of hunger, appetite and satiety were recorded. The subjects had been requested to abstain on test days from taking food between meals. Care was taken to avoid repeating like tests on a subject on successive days.

The investigation here reported was supported in part by a grant from the Department of Agriculture of the State of California (Wine Advisory Board).

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The experiments with tannic acid were carried out with the cooperation of 8 subjects. There were 140 test days on which the subjects observed customary food habits, 40 test days on which the subjects ingested a solution of tannic acid in water (150 cubic centimeters of 0.3 per cent solution of tannic acid U.S.P. in water) during noon meals and 25 test days on which the subjects (5 subjects) ingested the solution of tannic acid at lunch time in lieu of their noon meal.

The experiments with tartaric acid were carried out with the cooperation of 6 subjects. There were 93 test days on which the subjects observed customary food habits and 36 test days on which the subjects ingested a solution of tartaric acid in water (150 cubic centimeters of 0.5 per cent solution of tartaric acid U.S.P. in water) during noon meals.

The experiments with acetic acid were carried out with the cooperation of 7 subjects. There were 127 test days on which the subjects observed customary food habits, 42 test days on which the subjects ingested a solution of acetic acid U.S.P. in water) during noon meals and 61 test days on which the subjects ingested the solution of acetic acid at lunch time in lieu of their noon meals.

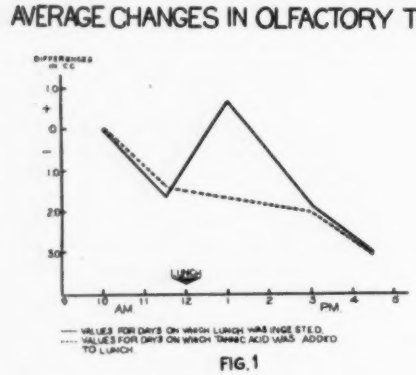

FIG. 1

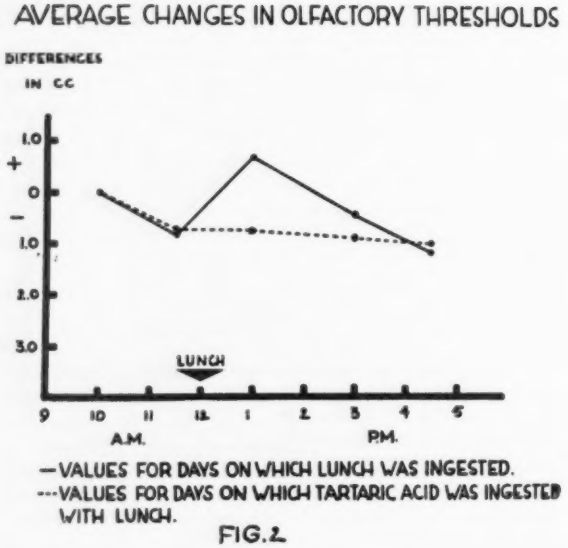

FIG. 2

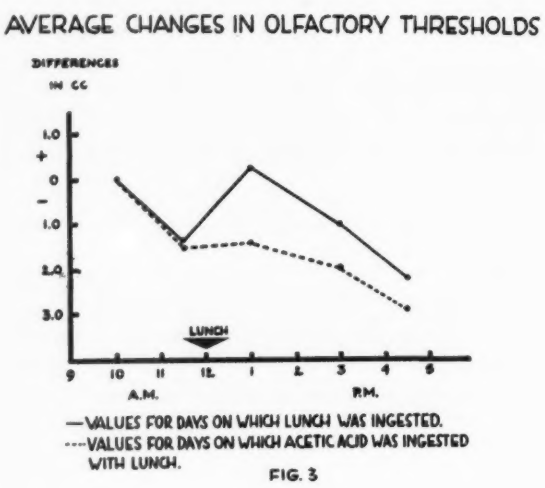

FIG. 3

RESULTS AND OBSERVATIONS

The results obtained are illustrated in figures 1, 2, 3, 4 and 5 and expressed in terms of average changes in olfactory threshold values taking the averages of values obtained at 10 o'clock in the morning as point of reference. It was justified to present the results in this manner because they were uniform for the various types of tests on all occasions.

Figures 1, 2, and 3 illustrate the changes in olfactory threshold values which occurred after ingestion of freely selected noon meals and after ingestion of freely selected noon meals supplemented with tannic acid solution (Fig. 1), tartaric acid solution (Fig. 2), and with acetic acid solution (Fig. 3) respectively. As can be seen, an increase of olfactory threshold values occurred following ingestion of freely selected meals while no increase of olfactory threshold values occurred following ingestion of freely selected noon meals supplemented with either of the acid solutions.

Figures 4 and 5 show that the tannic acid solution (Fig. 4) and the acetic acid solution (Fig. 5) ingested in lieu of noon meals were incapable of bringing about an increase of olfactory threshold values. Therefore the threshold values obtained after ingestion of freely selected noon meals differed from those obtained after ingestion of either of these acid solutions.

The results obtained for individual subjects were subjected to statistical analysis. The results of these

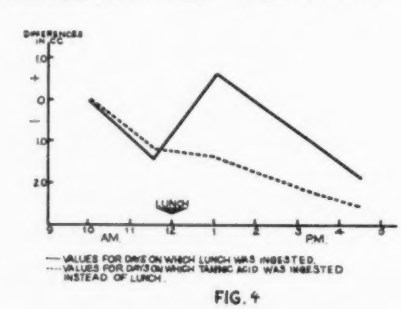

FIG. 4

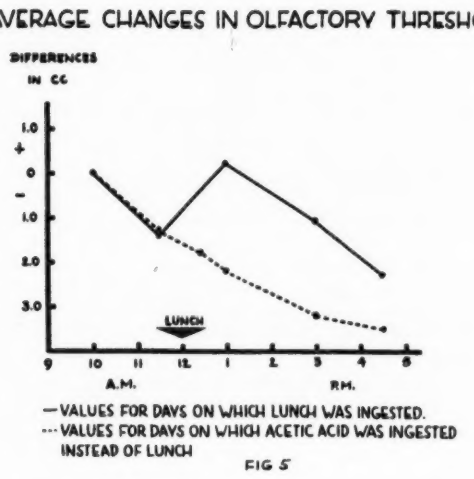

FIG 5

calculations are presented in tables 1, 2, 3, 4 and 5. In these tables the values in Columns B_1 and B_2 represent the average differences expressed as cubic centimeters of odorous air between threshold values obtained shortly before and after ingestion of noon meals (B_1) and shortly before and after ingestion of noon meals supplemented with acid solution or shortly before and after ingestion of acid solution (B_2) respectively. The values in columns P indicate the probability (calculated by means of Student's (6) t value) that the differences between the differences referred to are not significant. Applying statistical conventions, values of 0.05 or less are to be considered indicative of significance. This means that a difference is significant if the probability that it is not significant is 0.05 or less. Table I shows that the differences between olfactory threshold values obtained shortly before and after ingestion of noon meals differed significantly for all subjects from the differences between olfactory threshold values obtained shortly before and after ingestion of noon meals supplemented with the tannic acid solution. Tables II and III show that the differences referred to were significant for all but two subjects respectively in the case of tartaric acid (Table II) and that of acetic acid (Table III). Tables IV and V show that the differences between olfactory threshold values obtained shortly before and after ingestion of noon meals differed significantly for all subjects from the differences between olfactory threshold values obtained shortly before and after ingestion of the tannic acid solution (Table IV) and the acetic acid solution (Table V).

From the subjects' statements it was learned that the sensation of satiety created by meals supplemented with any one of the acid solutions was of markedly less intensity and shorter duration than that created by freely selected meals without such supplement. On days on which an acid solution had been ingested dur-

TABLE I

INGESTION OF TANNIC ACID WITH LUNCH

Average Differences Between Olfactory Threshold Values Obtained Before and After Lunch Time (expressed as c.c. of odorous air)

Subject	Number of Test Days on Which Lunch Was Ingested	Number of Test Days on Which Tannic Acid Was Ingested With Lunch	Difference B_1	Difference B_2	P
a	25	5	+2.0	−1.4	<0.01
b	22	5	+1.4	+0.2	<0.01
c	18	5	+2.6	−1.0	<0.01
d	21	5	+2.1	−1.0	<0.01
e	20	5	+2.85	+0.4	<0.01
f	12	5	+1.3	−0.6	<0.01
g	12	5	+1.9	0	<0.01
h	10	5	+1.8	+0.4	<0.05

TABLE II

INGESTION OF TARTARIC ACID WITH LUNCH

Average Differences Between Olfactory Threshold Values Obtained Before and After Lunch Time (expressed as c.c. of odorous air)

Subject	Number of Test Days on Which Lunch Was Ingested	Number of Test Days on Which Tartaric Acid Was Ingested With Lunch	Difference B_1	Difference B_2	P
i	8	6	+0.6	0	<0.20
j	19	6	+1.1	0	<0.01
k	20	6	+1.5	−0.1	<0.01
l	20	6	+1.0	0	<0.01
m	19	6	+1.3	+0.3	<0.10
n	7	6	+0.8	0	<0.01

TABLE III

INGESTION OF ACETIC ACID WITH LUNCH

Average Differences Between Olfactory Threshold Values Obtained Before and After Lunch Time (expressed as c.c. of odorous air)

Subject	Number of Test Days on Which Lunch Was Ingested	Number of Test Days on Which Acetic Acid Was Ingested With Lunch	Difference B_1	Difference B_2	P
o	16	6	+1.4	+1.0	<0.30
p	23	6	+1.1	+0.4	<0.20
q	16	6	+1.4	+0.1	<0.01
r	17	6	+1.3	−0.3	<0.01
s	12	6	+1.5	0	<0.01
t	25	6	+1.6	+0.1	<0.01
u	18	6	+3.1	−0.1	<0.05

TABLE IV

INGESTION OF TANNIC ACID IN LIEU OF LUNCH

Average Differences Between Olfactory Threshold Values Obtained Before and After Lunch Time (expressed as c.c. of odorous air)

Subject	Number of Test Days on Which Lunch Was Ingested	Number of Test Days on Which Tannic Acid Was Ingested in Lieu of Lunch	B_1 Difference	B_2 Difference	P
a	25	5	+2.0	+0.2	<0.01
b	22	5	+1.4	+0.6	<0.02
d	21	5	+2.1	−1.0	<0.01
e	20	5	+2.85	+0.6	<0.01
f	12	5	+1.3	0	<0.02

TABLE V

INGESTION OF ACETIC ACID IN LIEU OF LUNCH

Average Differences Between Olfactory Threshold Values Obtained Before and After Lunch Time (expressed as c.c. of odorous air)

Subject	Number of Test Days on Which Lunch Was Ingested	Number of Test Days on Which Acetic Acid Was Ingested in Lieu of Lunch	B_1 Difference	B_2 Difference	P
o	16	10	+1.4	−0.2	<0.01
p	23	8	+1.1	−0.2	<0.02
q	16	10	+1.4	−0.4	<0.01
r	17	8	+1.3	−0.5	<0.01
s	12	9	+1.5	−0.2	<0.01
t	25	10	+1.6	−0.3	<0.01
u	18	6	+3.1	−1.6	<0.01

ing noon meals the subjects found it difficult to abstain from taking food during the remaining hours of the day. Ingestion of the tannic or the acetic acid solution in lieu of noon meals was never noted to be followed by a sensation of satiety.

DISCUSSION

Changes in olfactory threshold values indicate changes in olfactory acuity. Thus decreasing threshold values signify an increase, increasing threshold values a decrease in acuity.

Therefore, the results of the present experiments show, in agreement with observations previously reported, that meals are preceded by a period of increasing and followed by one of decreasing olfactory acuity and that this decrease in olfactory acuity may be useful for estimating the ability of food to create a sensation of satiety. In addition, the results indicate that the acids under investigation, ingested during freely selected meals in the doses employed, prevent the postcibal decrease in olfactory acuity and interfere with the conversion by freely selected meals of sensations interpreted as desire for food into sensations interpreted as satiety afforded by food. When ingested in lieu of meals neither the tannic acid solution nor the acetic acid solution was found to be capable of demonstrably influencing olfactory acuity.

The described effects of the acids under investigation resemble quite closely those of bitter tonics (7). In studies concerning the assumed appetite-stimulating effect of bitter tonics ("Angostura Bitters") it was noted that these tonics ingested during freely selected noon meals prevent postcibal decrease in olfactory acuity and render freely selected meals incapable of bringing about the conversion of sensations interpreted as desire for food into sensations interpreted as satiety afforded by food. When ingested between meals bitter tonics were found to be without influence upon olfactory acuity, upon the sensations in question and upon the caloric value of succeeding meals. The failure of bitter tonics to influence in normal individuals precibal changes in olfactory acuity and to intensify the sensations interpreted as desire for food, was explained by assuming refractoriness to augmentation of precibal increase in olfactory acuity and of intensity of the desire for food, both presumably of optimal magnitude. The resemblance of these results with those of the present experiments and the fact that the acids studied represent constituents of bitter extracts suggest that the acids may be responsible in part for the effects ascribed to bitter tonics. If the described effects of bitter tonics can be shown to represent an expression of the "appetite-stimulating" effectiveness commonly ascribed to bitter agents, it would be justified to ascribe such effectiveness also to the acids in question. The ability of these acids to prevent creation of sensations interpreted as satiety may be regarded as lending physiological significance to the wide spread occurrence of these acids in food and drink. The mode of action responsible for these effects of tannic, tartaric and acetic acid cannot be explained at this time.

In connection with the preceding report on experimental studies it appears justified to comment briefly on preliminary studies concerning the influence of wine upon olfactory acuity and sensations associated with food intake. The demonstration in experiments that certain constituents of wine—as alcohol and sugar—are capable of depressing sensations interpreted as desire for food (8, 9), while certain other constituents of wine—as tannic, tartaric and acetic acid—are capable of preventing creation by food of sensations interpreted as satiety led to the assumption that the influence of wine upon the sensations in question may depend upon the composition of the wine. There is widespread belief that wine may be useful as an "appetite-stimulating" agent. In view of the information referred to above it was decided to investigate the influence dry wine may have upon olfactory acuity and sensations associated with food intake. These studies are being carried on with the cooperation of individuals in apparently good health and with that of individuals suffering from anorexia due to different causes. Although these studies are incomplete at this time, certain observations were made which appear worthy of mention.

It was noted that dry wine (100 cubic centimeters)

ingested during freely selected meals is capable in normal individuals of simultaneously preventing the postcibal decrease in olfactory acuity and of diminishing intensity and duration of sensations interpreted as satiety afforded by food. These effects of wine could be demonstrated by using either red or white dry wine.

In addition it was observed that diurnal variations in olfactory acuity fail to occur in individuals suffering from anorexia. The absence of diurnal variations in olfactory acuity was found to be independent of the cause of anorexia. In individuals suffering from anorexia dry wine ingested at meal time was noted to be capable of producing an increase in olfactory acuity accompanied by sensations which might be interpreted as a desire for food. On occasions it was noted that individuals so treated ingested at succeeding meal times an amount of food larger than expected. Statistical analysis of results obtained in these studies as well as conclusions on the subject cannot be presented as yet. Suffice it to say that the observations made so far warrant and justify further investigations along these lines. The difficulties involved in investigations of this type are obvious.

SUMMARY

Experiments are described which demonstrate that tannic, tartaric and acetic acid ingested during meals are capable of simultaneously preventing postcibal decrease in olfactory acuity and interfering with creation of sensations interpreted as satiety.

The suggestion is made that the effects of the acids mentioned may be related to the appetite stimulating effectiveness commonly ascribed to bitter tonics and to dry wine.

Mention is made of preliminary clinical investigations which indicate that dry wine may be a useful adjunct in the treatment of anorexia.

The clinical studies are incomplete at this time.

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ABSTRACTS ON NUTRITION

DRUMMOND, SIR JACK: *Nutritional problems and civil defense.* Pub. Health Reports, 67, 9, Sept. 1952, 857-859.

Drummond summarized his concepts of the title subject by stating that, under conditions of stress, attention should be concentrated primarily on the provision of energy. Apart from the special case of mothers and children, other nutritional requirements are of quite secondary importance. It is also highly important that the foods to be distributed should be palatable and acceptable. It is far more important to give people an emergency food they wish to eat than to offer them something that is nutritious but unappetizing.

WALKER, S. H.: *Ineffectiveness of carob flour in infantile diarrhea.* Amer. J. Dis. Child., 84, 3, Sept. 1952, 309-315.

A controlled study of 47 cases of infantile diarrhea in which alternate patients were treated with carob flour is reported. The findings indicate that this substance does not significantly alter the course of the diarrhea or the concomitant loss of stool fluid. Carob flour has a high lignin and pectin content. Other investigators had considered that carob flour exerted an antidiarrheal effect.

CHARI, N. V.: *Malnutrition among children in Madras.* The Antiseptic, XLIX, 6, June 1952, 435-441.

Malnutrition in children is a very serious problem in India, particularly in the South where rice forms the chief staple of diet, as contrasted with the North where wheat takes its place. Ignorance, poverty and round worm infestation are abetting causes. In Madras, blindness in children is usually due to avitaminosis. The "nutritional edema syndrome" is the same as Kwashiorkor in Africa. There is also a marasmic group of wasted children. In some cases of malnutrition in children, edema is the only evidence, and this is called the "famine edema" group, and they respond dramatically to intravenous protein hydrolysates. Pellagra is rare in India. The critical period is that of weaning. Some women nurse their babes for 3 years when cow's milk cannot be attained. Hypoproteinemia plays a very important part in malnutrition in the children in Madras, largely because a rapidly increasing

birth rate has outstripped the production of protein foods.

DEWIND, L. T., MICHAELS, G. D. AND KINSELL, L. W.: *Lipid studies in patients with advanced diabetic atherosclerosis.* Ann. Int. Med., 37 No. 2, 1952, 344-351.

Twenty-four cases of diabetic arteriosclerosis were studied to determine the effects of lipotropic agents on the insulin requirements and the lipid blood levels. No correlation between any of the lipid values estimated and the atherosclerotic process was found, although the mean serum cholesterol values were significantly higher than in a group of non-diabetic elderly controls. The use of rather large amounts of inositol or choline did not produce any significant changes in blood lipids, nor was there any significant change in the diabetic state. In several patients receiving testosterone propionate, 25 mg. daily, there occurred a depression of serum cholesterol esters, serum phospholipids and serum lipoprotein, as well as some change in insulin requirements, but these changes were not constant.

FREED, S. C. AND MIZEL, M.: *The use of amphetamine combinations for appetite suppression.* Ann. Int. Med., 36, 6, June 1952, 1492-1497.

In some patients, dextro-amphetamine has little effect in suppressing appetite. These so-called "vagotonic" persons do better on the racemic form, due perhaps to its levo-amphetamine content. The levo-form has little effect *per se* on the appetite but may act as a "sensitizer" to the appetite-suppressing action of the dextro-amphetamine. A combination of the amphetamines containing a ratio of 1:3 of levo-to-dextro- is the most effective one.

FINBERG, L. AND CHOW, B. F.: *Lack of effect of supplementary vitamin B_{12} administered to premature infants.* Am. J. Dis. Child., 84, 2, Aug. 1952, 165-167.

Daily administration of an oral supplement of 30 micrograms of vitamin B_{12} produced no demonstrable effect upon premature infants with regard to growth or hematological status. There is no justification for the routine use of this substance in premature care.

BRINKMAN, G. L.: *Nutritional heart failure.* New Zealand Med. J., LI, 283, June 1952, 173-177.

In a very thoughtful article, which should be read carefully in the original, Brinkman describes 3 or 4 unfamiliar forms of cardiac failure due, presumably, to faulty nutrition. There is, first, a subacute form of vitamin B_1 deficiency (not to be confused with beriberi) which does not injure the peripheral nerves but gradually leads to cardiac damage of an irreversible type, so that treatment with thiamine has no effect. These cases are characterized by a greatly enlarged heart which at autopsy shows endocardial fibrosis, with adherent thrombi, and scattered areas of hydropic degeneration of the myocardium, but no myocarditis.

A second type is somewhat similar, with endocardial fibrosis, no myocardial changes but always an eosinophilia. Such cases have been described in natives of East and West Africa and are almost certainly of nutritional origin, although thiamine is not lacking. Sometimes this second type has occurred in well-nourished Europeans.

There is a third type among the Bantus of South Africa. Congestive failure is resistant to thiamine, but the use of a good varied diet results in rapid improvement.

There is a fourth type among the younger Indian population of Suva. Thiamine is ineffective, but nevertheless these cases may represent resistance to the very vitamin whose lack (during alcoholism especially) was responsible for the disease.

Brinkman thinks that the process of endocardial fibrosis, once initiated, becomes self-perpetuating. This may explain the death of a man from congestive cardiac failure who was exposed to four years of starvation, but only lived four years after resuming a normal diet.

HAUNZ, E. A.: *Successful management of the diabetic patient.* Journal-Lancet, Oct. 1952, 461-469.

Haunz, from his obviously extensive experience with diabetes, selects a number of points for profitable discussion. One is that the majority of diabetics must be discovered by the general practitioner. He describes the "purists," "middle of roaders" and the "free dieters," places most confidence in the teachings of the Boston group, but thinks that more time will be required to know whether the Tolstoi school are really doing any harm to patients. Haunz used short movie reels to educate new or uncooperative patients. In obesity he withholds insulin, where possible, during the process of weight reduction because insulin stimulates appetite. He decides by trial and error methods which type of insulin to use, being impressed with the universality of application of N.P.H. except in the most "brittle" cases, where he uses multiple doses of regular insulin. In using Lilly's strong (1 c.c. equals 500 units) insulin in insulin resistance, he warns that the resistance may suddenly disappear, thus giving rise to dangerous hypoglycemia. He favors the Somogyi-Nelson method of blood sugar estimations.

ZELMAN, S.: *The liver in obesity.* Arch. Int. Med., Aug. 1952, 99, 141-156.

Twenty obese men, between 50 and 100 percent overweight, who had never had liver disease, were studied for liver disturbances by function tests and needle biopsies. In none was the liver found to be entirely normal. There is a greatly increased incidence of hepatic cirrhosis in the obese as revealed by insurance statistics. The reducing program should consist of a high-protein diet supplemented by choline and vitamins of the B complex.

WOODHILL, J. M.: *The diets of a group of pregnant women living in Sydney.* Med. J. Australia, 39, II, 6, Aug. 9, 1952, 192-196.

Using Burke's Dietary History Method (Harvard Group), Woodhill investigated the diets of 186 pregnant women with special reference to the following nutrients, calories, protein, calcium, iron, vitamin A and/or available carotene, thiamine, riboflavine, niacin, and ascorbic acid. Prior to pregnancy, 15 percent of the group were eating diets which, in respect to the nine nutrients calculated, were less than 50 percent of the National Research Council's (U.S.A.) recommended

daily dietary allowances. These faulty diets were not related to poverty but rather to periodic scarcities of essential foods and the rising costs of foods. An important public health objective should be the education of young women in good dietary habits in preparation for pregnancy, since some of the diets studied would decrease the chances of having a completely successful pregnancy and lactation period.

FOX, J. R.: *The incidence of diabetes mellitus and glycosuria in 19,358 college students.* Journal-Lancet, Oct. 1952, 479.

In screening 19,358 college students at the University of Minnesota Health Service, 155 glycosurics were found. No less than 70 cases of diabetes were found. Renal glycosurics totalled 32. There were 47 cases of glycosuria with a normal blood sugar curve and no evidence of renal abnormality, which were classed as normal variance. There were 6 cases of so-called "temporary hyperglycemic glycosuria" in whom the fasting blood sugar was normal, the blood sugar peak high, but the return to normal of the curve was definite in an hour and a half. Of the diabetics, 48 were male and 22 female. The diabetic females were overweight while the males were normal or underweight.

EDITORIAL

HEART PAIN AND GASTROINTESTINAL ABNORMALITIES

There are so many instances in which the cardiologist and the gastroenterologist are likely to disagree on a diagnosis that one scarcely knows where to begin his description. Otherwise expressed, an internist is almost daily confronted with the problem, "are these symptoms arising above or below the diaphragm, or, indeed, *in* the diaphragm itself?" There is a medically popular feeling that when a patient complains of his stomach his real trouble is in his heart and that when he blames his heart, his stomach is the real cause. Such a popular feeling possesses only one advantage—it keeps the internist in an inquisitive mood. The pain of coronary occlusion sometimes is referred chiefly to the epigastrium, but the cardiogram usually makes the differentiation. In patients who are not very ill, substernal distress may be completely relieved by belching. Unfortunately, angina pectoris may exist in the presence of a normal cardiogram and a normal chest film, and there is too much of a tendency nowadays to brush off the diagnosis under such circumstances. Time and time again a patient with anginal symptoms but without x-ray or cardiographic abnormalities has dropped dead a few days after the initial examination.

Perhaps every one of us has been guilty of overlooking a diseased gallbladder, which when finally removed, caused a complete cessation of the angina. The spastic colon itself is unquestionably capable of producing substernal pain referred to the left arm, *apparently* as a result of gaseous distention and pressure against the diaphragm. Possibly "the splenic flexure syndrome" deserves special recognition in this connection (1).

Finally, it should be stated that diaphragmatic hernia, hiatus hernia and eventration of the abdominal viscera into the chest are not uncommon conditions, but they are, unfortunately, usually overlooked, except by the well-trained roentgenologist. They are capable of producing substernal pain referred to the left arm, especially after meals. In some cases at least they appear to induce a reflex but genuine angina pectoris.

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BOOK REVIEWS

THE ESOPHAGUS AND ITS DISEASES. Eddy D. Palmer, M. D. Paul B. Hoeber, Inc., New York, N. Y.

Eddy Palmer, who has contributed so much valuable material to gastro-enterology, now places us under further obligation by producing the best volume on esophageal diseases that has yet appeared. As he states, the ground work for all future advances, by perfecting of the endoscopic technique, has been contributed by the laryngologists, although the radiologist is responsible for complementary diagnostic methods. The gastroenterologist now is attempting to take over the esophagus and its diseases and it is true that many medical diseases affect this organ. The various abnormal conditions of the esophagus become increasingly important to diagnose since modern surgery is now capable of dealing successfully with certain of the organ's more important diseases. The text, which runs to more than 550 pages, is well illustrated, and covers the uncommon as well as the common pathological conditions affecting the esophagus. Extensive references are included in each chapter. Every internist, not to say every gastro-enterologist, will profit greatly from a careful study of Palmer's book.

KITCHEN STRATEGY. (The Family Angle on Nutrition). Leona M. Bayer, M. D. and Edith Green. Charles C. Thomas, Springfield, Illinois. $3.75.

Strategy in the kitchen aims to convert modern nutritional knowledge into good eating habits for the family. As Ernst Wolff comments, in the foreword, food is the most important environmental factor af-

fecting health. High prices for food and seasonal and regional scarcities are the two factors interfering with the mother's plan for adequate meals. The mother is shown, in this popular book, what are the recommended daily food allowances, also how she may safely substitute one food for another. The means given for common ailments, such as colds, diarrhea, constipation, and simple anemia are valuable and unobjectionable. This is a book which should be recommended to mothers by the physician who possesses a sense of the great importance of improving family nutrition.

NUTRITION IN THE PRACTICE OF MEDICINE. J. Arnold Bargen, Paul R. Cannon, John B. Condliffe, Perry J. Culver, Robert M. Kark, Heinrich Necheles and Frederick J. Stare. The National Vitamin Foundation, Inc., 150 Broadway, New York 38, N. Y., 1952, $1.50.

The contents of this book represent the proceedings of the Nutrition Symposium held at the University of California, School of Medicine, San Francisco, Oct. 30, 1951. The chief subjects dealt with are intestinal absorption, liver disease, pancreatic insufficiency, ulcerative colitis, tissue devitalization, tissue changes caused by deficiencies, and international economic aspects of nutrition. Intestinal absorption is a very complicated process, and we shall never arrive at a mathematical formula to explain it. Thiamine absorption may be limited to 5 mg. daily. Iron may be refused absorption if it is not needed. There is competition between the intestinal flora and the host for vitamins, particularly in achylia. The paper by Necheles on pancreatic insufficiency is extremely interesting. Bargen, as always, sheds light on the treatment of ulcerative colitis. The book should be read by all physicians.

GENERAL ABSTRACTS OF CURRENT LITERATURE

BUCAILLÉ, MAURICE: *Duodeno-colic Fistulas.* Arch. mal. app. dig. et mal, nutr. 41, 6, 643. June 1952.

Duodeno-colic fistulas are very rare. They may be due to a benign cause (non neoplastic) or to a malignant (neoplastic) cause.

1. *Benign duodeno-colic fistula*: two cases are reported by the author, one of them subordinate to an operatory traumatism involving both the duodenum and the colon in the course of an extremely laborious operation for acute intestinal obstruction, the other subordinate to an old lithiasis of the gall-bladder through perforation of the gall-bladder into both the duodenum and the colon.

In connection with these two new cases, the author has gone over the cases of duodeno-colic fistulas published up to now (17). He describes the different possible locations, the anatomical characteristics, the different causes, the clinical symptoms which are the result, on the one hand, of the brusque entry of food into the colon and also of the passage of the contents of the colon into the duodenum, and, on the other hand, of the insufficient digestion of foodstuffs. Then he goes on to study their radiological diagnosis. He criticizes the different surgical methods of treatment practiced. The following results were obtained: 2 deaths and 13 recoveries out of 15 cases operated on.

2. *Malignant duodeno-colic fistulas.* (18 cases chosen out of the existing literature, 8 of which being discovered at the autopsy). These are practically all subordinate to a perforation of a cancer of the colon into the duodenum.

A detailed study is made from the etiological, anatomical, clinical and radiological point of view.

Surgical treatment is extremely difficult, calling for the total resection of the tumor of the colon and of the affected duodenum. The author explains the technique used by Linton and emphasizes the excellence of his results due to the use previously of double gastric and colic leads.

Of the 10 patients operated upon by different authors, 40% recovered from the operation (2 out of 2 for Linton).

CACHERA, R., DEBRAY, C. AND DARNIS, F.: *Gastrectomy and gastro-jejuno-colic fistula in children. Nutritional and endocrine after effects.* Arch. mal. app. dig. et mal. nutr. 41, 6, 605. June '52.

The case of gastro-jejuno-colic fistula studied in this paper adds to the list of sequelae and complications following gastrectomy. It includes disorders of exceptional intensity due to the fact that gastrectomy was performed at the age of 7. For this reason, important endocrine irregularities are added to the well-known nutritional disorders.

1. Malnutrition reached an extraordinary degree similar to that observed in deportee camps; but its evolution extended over a longer period and started at an earlier age than in the case of undernourished prisoners. Serious cachexia was accompanied by fundamental irregularities in serum proteins. The very marked reduction of these (44 gr. per 1,000) affected both the albumin and the globulin ($\frac{A}{G} = 1.33$). But the reduction in concentration was not yet sufficient indication of the real loss suffered by the protein content of the blood. Actually the volume of plasma was greatly reduced as in the conditions known as "chronic shock": in such a way that the total quantity of circulating protein, as well as the total blood cell volume fell to figures which were unprecedented in the author's experience.

2. It should be noted that no important edema appeared with this patient whose extra-cellular liquids were diminished in comparison with the theoretical weight.

3. Glucids, total lipids, cholesterol were likewise greatly reduced.

4. There was a marked polyendocrine deficiency, notably genital and of the adrenal cortex, in addition to malnutrition. The condition reached was that of cachectic infantilism.

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A remarkable fact was recorded in this instance: testosterone and desoxycorticosterone administered in massive doses failed to produce their customary effect, the receptors giving only an insignificant response in this undernourished patient.

5. One point of great importance must finally be emphasized: the existence in this patient of a massive hepatic steatosis.

The histological appearance was analogous to the lesions of dietetic origin produced experimentally in rats, or observed in humans of certain countries as a consequence of diets deficient in protein; and it was also similar to that of the liver in alcoholics.

The formation of cirrhoses which develop on a fatty infiltrated liver therefore raises histogenetic problems similar to those following on nutritional or endocrine etiology.

6. The evolution of nutritional and endocrine disorders together with hepatic lesions after a surgical cure of the fistula was at first favorable. Specially, after needlebiopsy there could be noticed a considerable regression of the steatosis.

CAROLI, J., TANASOGLU, Y. AND COHEN, M. *The Bromsulfalein appearance-time in bile. Its diagnostic value in incomplete obstructive jaundice and in non icteric obstruction of the common bile duct.* Arch. mal. dig. app. 41, 6, 623. June '52.

The B. S. P. appearance time in Bile is not a laboratory procedure but a simple clinical method. Its measurement is made by the combination of duodenal intubation with the usual intravenous injection of B. S. P. (150 mg per square meter). For this purpose, the biliary fluid is simply collected by syphonage into butes containing a few drops of 10% sodium hydroxide solution; these tubes are shaken every minute until a reddish-violet color develops. In order that the test be reliable: a) the output of biliary juice must be sufficient (about 1 cc per minute as an average) and b) it must contain a detectable amount of bile. Moreover the biliary flow can be stimulated by intraduodenal instillation of novocain or magnesium sulfate.

In normal subjects, the B. S. P. appearance time ranges between 5 and 15 minutes. This test is of significant value in uncommon cases of subtotal and yet latent common bile duct obstruction. In these instances (5 cases) not only is the B. S. P. retained in the blood, but the appearance time of B. S. P. in bile is very delayed (from 30' to 50') despite an apparently normal biliary output. On the contrary, in *cirrhosis of the liver*, the B. S. P. appearance time is shortened from 5' to 8' (10 cases). Unfortunately, most of the latent common bile duct calculi impair neither the biliary flow, nor the B. S. P. appearance time.

The test is diagnostically the most informative in incomplete obstructive jaundice. In hepatitis with jaundice (16 cases) the B. S. P. appearance time is normal or shortened; exceptions are encountered only when a complete intrahepatic occlusion to the bile flow is present. It is the only reliable test in those cases of hepatitis with biological data of pure biliary stasis (4 cases). The test also retains its value in cirrhosis with jaundice (2 cases).

In the course of jaundice due to incomplete common bile duct obstruction (caused by lithiasis, pancreatitis, post operative stricture, carcinoma of the papilla major) despite an important biliary output, a marked delay in the appearance time of B. S. P. is however recorded. Of great interest is the test in case of cholostatic cirrhosis (1 case).

Whether jaundice is present or not, there are two main types of B. S. P. retention in the blood: 1) retentions by parenchymal hepatic damage associated with a B. S. P. elimination time normal or shortened; 2) retentions due to common duct obstruction with a prolonged B. S. P. appearance time in bile.

The B. S. P. retention due to parenchymal lesion seems related to functional impairment on the vascular side of the hepatic cell. But any particle of the dye reaching the biliary duct system rapidly goes into the duodenum. In cirrhosis, the quickened rate of dye elimination may be due to an increase in the biliary output, to shortening of the liver cell cords and to proliferation of numerous new bile canaliculi; in the course of hepatitis with jaundice, even though one agrees with our own hypothesis of mechanical obstruction of the canals of Hering, nevertheless a sufficient number of biliary passages remain open, so that the bile and the dye flow rapidly through biliary ducts, when the pressure is low.

In jaundice due to incomplete common bile duct obstruction, the B. S. P. blood retention is related to functional inhibition of the biliary side of the hepatic cell, because of over-pressure in the excretory system. But, in that case, this effect is uniformly spread out over the whole hepatic parenchyma, which explains the delay in the appearance-time of the dye in the duodenum.

CHARRIER, J., LOYGUE, J., TIRET, M.: *Development of the treatment of cancers of the descending colon.* A study of a series of 125 cases. Arch. mal. app. dig. 41, 6, 593. June '52.

This work is based on the study of 125 cases of cancer of the descending colon (including the splenic flexure, excluding the rectum) operated on by them between 1930 and 1951 and having undergone exeresis by different methods. These cases are divided into two series:

1. from 1930 to 1946
2. from 1946 to 1951

In the second series, use was made of modern antibiotics, internal disinfection by sulfonamides (succinylsulfa-thiazol) and general antibiotics, first of all penicillin and later streptomycin and aureomycin. The results achieved show an improvement on operatory results, a fact which has enabled us to abandon almost completely amputations in several stages and after 1946 to perform operations in a single stage without previous leads.

First Series.

Forty-two cases between 1930 and 1946. The methods used were in particular a) exteriorization with resection after 6 to 8 days then subsidiary closure of the anus after several weeks in 16 cases; b) exteriorization and immediate resection with delayed closure as above in 15 cases; c) artificial anus for obstruction or

infection, then exteriorization and resection followed by closure of the anus in 10 cases. Operatory mortality rate at the different stages was 14 out of 42, that is 35% due in particular to post-operatory infection, peritonitis, cellulitis or cachexia. The delayed after-effects on 21 patients operated on and who have been traced since are:

8 deaths due to metastasis or relapse

5 deaths from other diseases

8 still alive 5 to 12 years afterwards.

But out of the total, 12 survived longer than 5 years.

Second Series.

83 cases from 1946 to 1951. The methods used are:

a) exteriorization, resection and closure in 2 or 3 stages for 3 cases

b) artificial anus first of all (at a distance, beneath the splenic flexure or cecal) for obstruction or infection, then resection and immediate anastomosis and closure of the anus in a third stage: 14 cases.

c) resection and immediate anastomosis in one stage: 66 cases. (With immediate fistulization above or cecal fistulization often at the beginning but much less frequent now).

Immediate mortality was 5 out of the total and 2 out of the 66 cases in one stage, that is 30%, the cause of death here was not due to infection but above all to the mechanical obstruction of the small intestine. The authors attribute this considerable improvement to:

1. Preparation and post-operative care with antibiotics.

2. The management of the operation: wide exeresis, minute reconstruction of the whole of the peritoneal plane, septic stage left until the end, drainage behind or beneath the peritoneum.

3. By the elimination of all mechanical causes of obstruction by the obturation of all abnormal intra-abdominal orifices created by the exeresis.

The delayed after-effects are too recent: all those operated on have been traced. At the end of 1951 the following were still alive:

2	patients out of 2	operated on in	1946
5	 7	.....	1947
7	 16	.....	1948
13	 14	.....	1949
15	 16	.....	1950
11	 11	.....	1951

Against post-operatory obstruction, always of the small intestine, often masked by the antibiotics and intestinal aspiration, they advise immediate reoperation after an early radiological diagnosis.

MAITLAND, D. G.: *The limitations of Graham's test in the examination of the gall-bladder.* Med. J. Australia, Jan. 12, 1952, 43-44.

Where there is no history of biliary dyspepsia, the only positive report possible on the results of the Graham Test is the conclusive demonstration of gall-stones opaque or radiolucent. Maitland thinks the progress of contraction of the gallbladder, following a fatty meal is the more important part of the examination. Delay in contraction may be due to an unsuspected duodenal ulcer with pylorospasm. He thinks sluggish contraction probably indicates cholecystitis. He also thinks that a hardly perceptible shadow of the gallbladder indicates moderate cholecystitis. (On these points not all authorities agree.—Reviewer). It is useless to give the dye to a jaundiced patient. The intrinsic papilloma may be indistinguishable from small calculi.

BODIAN, M., WHITE, L. L. R., CARTER, C. O. AND LOUW, J. H.: *Congenital duodenal obstruction and mongolism.* Brit. Med. J., Jan. 12, 1952, 75-78.

In a consecutive series of 32 infants with congenital atresia or stenosis of the duodenum, a high incidence of Mongolism was observed. The frequency of this association has not been generally appreciated, because most children with duodenal obstruction die during the neonatal period, when Mongolism is likely to be overlooked. The early recognition of Mongolism in a newborn child with suspected duodenal obstruction may be of practical importance in managing the case. The features of Mongolism in the newborn are described.

SKINNER, H. H., EDMARK, K. W., BAKER, J. W., STONE, C. S. AND OWEN, J. G.: *A review of surgery of the stomach and duodenum for 1951.* Bull. Mason Clin., 6, 1, March 1952, 1-9.

The authors review 75 cases of surgical operations on the stomach and duodenum for 1951, including 60 benign and 15 malignant lesions. There were two post-operative deaths both occurring after total gastrectomy for gastric cancer. They favor partial gastrectomy for benign ulcer of the stomach, pylorus or duodenum with a Billroth I anastomosis when possible. For gastric cancer, they prefer total gastrectomy with splenectomy and omentectomy. The average age of all patients with gastric or duodenal lesions (benign or malignant) falls in the 50-55 year old age.

SKINNER, H. H. AND STONE, C. S.: *A subdiaphragmatic abscess with benign gastric ulcer simulating carcinoma.* Bull. Mason Clin., 6, 1, Mar. 1952, 30-35.

A 61 year old man who had previously been operated on for a perforation of a gastric lesion was said to have liver metastases, and x-ray studies suggested a large cancer of the lesser curvature. Re-operation revealed a gastric ulcer and a subdiaphragmatic abscess on the left side. A subtotal gastrectomy was done and the abscess evacuated. He made a good recovery. The cases illustrate how difficult it may be to differentiate between a malignant and a benign lesion without operation and biopsy.

GABRIEL, W. B.: *The surgical treatment of chronic ulcerative colitis.* Brit. Med. J., April 26, 1952, 881-885.

The important indications for surgery in chronic ulcerative colitis are, the failure of medical treatment, evidence of pseudopolyposis, and arthritis. When fibrosis and pseudo-polyposis are present, ileostomy and total colectomy give a good prospect of cure, provided that the radical operation is done *before* the onset of cancer. In a series of 68 cases treated surgically in the past ten years, cancer is known to have developed in six cases (9 percent). The average duration of the disease in these cases was 19 years. Gabriel recommends a 3-stage operation for total colectomy and in 50 such cases the mortality was 6 percent for ileosto-

my, 6.25 percent for subtotal colectomy and none for the final recto-colic excision. The rectal function should not be preserved, as the remaining rectal segment is likely later to become involved by the ulcerative process.

FUKUSHIMA, K.: *On the ion concentration of digestive juices.* Med. J. Osaka Univ., 2, 4, Oct. 1951, 67-70.

Working on dogs, the author determined the ion concentration of chlorine, sodium, potassium and the Cl:Na:K ration in gastric, intestinal and pancreatic juice, as well as bile, both before and after eating. Chlorine is highest in gastric juice and lowest in pancreatic juice and bile. Sodium is highest in gastric juice and lowest in intestinal juice. The sodium ions are lowest in gastric juice one hour after feeding, at a time when HCl is highest. He found the potassium ion concentration greater than the sodium ion concentration in gastric juice. The intestinal juice contains the largest quantity of potassium ions.

RIDDELL, H. J.: *Interdigestive gastric secretion in duodenal ulcer: a study of the comparative inhibition by hexamethonium iodide and L-hyoscyamine.* Brit. M. J., Dec. 22, 1951, 1498-1500.

Adequate doses—larger than are normally used—of belladonna, or its alkaloids, orally, and intramuscular hexamethonium iodide produce substantial inhibition of interdigestive secretion in patients with duodenal ulcer, comparing favorably with the effects of vagotomy. Belladonna was given in doses sufficient to produce dry mouth and blurring of vision. Belladonna (or its alkaloid L-Hyoscamine) had similar effects to those of hexamethonium iodide intramuscularly. Similar substantial reduction in secretion volume and acid and pepsin output was obtained with either drug.

STONE, C. T.: *Portal hypertension.* Amer. Pract. & Dig. Treat., 3, 2, Feb. 1952, 134-137.

Stone gives a brief but valuable review of the present status of portal hypertension. Naturally, as he states, the best treatment is prevention, by the successful treatment of early hepatic cirrhosis where this is possible. Spleno-renal venous shunt is not as valuable as porto-caval anastomosis (Eck fistula), but there is a high operative mortality in advanced cases. The simple operation of ligation of the splenic artery carries a very much lower mortality and appears to be successful. Stone sees reasons for being more optimistic today than ever before in treating the decompensated hepatic cripple.

HOERR, S. O. AND PERRYMAN, R. G.: *Catheter duodenostomy: a safeguard in gastric resection.* Cleveland Clinic Quart., 19, 2, April 1952, 49-56.

Catheter duodenostomy is a valuable maneuver in patients where technical difficulties render a tight closure of the duodenal stump difficult or insecure. The technic of the procedure is described, and 11 cases reported, among whom no deaths and no serious complications occurred.

GOULSTON, S.: *The value and limitations of x-ray examination in assessing disease of the gallbladder.* Med. J. Australia, Mar. 8, 1952, 323-325.

A normal cholecystogram does not rule out gallbladder disease—in 5 to 10 percent of such cases distinct gallbladder disease is present. The Graham test, however, when properly carried out, carries a high degree of accuracy. When the history and physical findings of gallbladder disease are clear-cut, there is scarcely any need of cholecystography.

JOLLEYS, A: *Death following a barium enema in a child with Hirschsprung's disease.* Brit. Med. J., Mar. 29, 1952, 692-693.

A diagnosis of megacolon was made on a boy of 3 by introducing 4 pints of barium emulsion, but he could not expel it and all efforts to retrieve the barium failed. His condition soon became unsatisfactory, he was cold, collapsed and sweating. Coma developed within 7 hours and he began to have generalized convulsions. He died in a convulsion 20 hours after the barium enema had been given. The author states cogent reasons for believing that death was due to water intoxication, which is known to be capable of producing cerebral edema. Hence the danger of water intoxication should be remembered when enemas are given to children with megacolon.

TSURUMARU, H.: *On the agastric syndrome after total gastrectomy.* Kyushu Memoirs of Med. Sci., 2, 3, Dec. 1951, 145-157.

The author notes edema, hypoproteinemia, alimentary glycosuria and hyperglycemia, hypoglycemic symptoms during hunger, and anemia, following total gastrectomy. He finds that edema and hypoproteinemia tend to occur 2 to 4 years after the operation and are likely to correct themselves.

TOMODO, M.: *Technique of substitute stomach formation after total gastrectomy.* Kyushu Memoirs of Med. Sci., 2, 3, Dec. 1951, 159-166.

In certain stomachless fish investigated by the author, the upper part of the intestinal tract is so formed as to perform the motor functions of the stomach. He has now successfully operated on 30 patients, doing total gastrectomies, and using a special technique by which a portion of the jejunum is narrowed-off and apparently works like a stomach. These patients thus far have had much fewer unfavorable symptoms following total gastrectomy than those who have undergone the usual operation.

GAINES, W., STEINBACH, H. L. AND LOWENHAUPT, E.: *Tuberculosis of the stomach.* Radiology, 58, 6, June 1952, 808-819.

From the x-ray standpoint, the tuberculous ulcer appears similar to chronic gastric ulcers of the peptic type. 73 percent of them are located in the pars media. Predominantly hyperplastic lesions have occurred more frequently (38 to 11) than ulcerative lesions. Three cases of gastric tuberculosis and one case of chronic gastric ulcer secondarily infected with T.B. are presented. An ulcer crater was demonstrated in all four cases. A definite diagnosis of gastric T.B. cannot be made by x-ray alone. But in a young person with an ulcer which fails to respond to medical treatment and who has evidence of T.B. elsewhere, the disease should be suspected, especially in persons of Negro or Mexican descent. When gastric T.B. is suspected, a therapeutic test with streptomycin for at least 3 weeks should be made.

REED, F. N.: *The physiology of intestinal obstruction.* Bull. Mason Clin., 6, 2, June 1952, 64-74.

Bowel obstruction today is an important disease responsible for a high percentage of hospital deaths. The seriousness of high obstruction is due to loss of electrolytes and fluid by vomiting. In low obstruction, the main symptoms and death result chiefly from the effects of bowel distention. Treatment must be directed toward prompt hydration, prevention and relief of distention and early release of the obstruction.

MCNEE, SIR JOHN: *Infective hepatitis: a problem of world health.* Brit. Med. J., June 28, 1952, 1367-1371.

McNee believes that homologous serum jaundice and syringe-transmitted hepatitis are one disease. The virus of acute infective hepatitis is now widely spread throughout the world. The disease occurs sporadically and in small outbreaks at frequent intervals, and has already exploded in real pandemic form (during the American Civil War). In these respects it resembles influenza. Future pandemic forms are possible. Thus it becomes a problem of world health.

TURNBULL, R. B., JR., AND MICHELS, A. G.: *The management of the patient with the permanent colostomy.* Cleveland Clinic Quarterly, 19, 1, Jan. 1952, 12-19.

The authors describe methods of periodic colonic lavage through the colostomy opening which does away with the need for a rubber receptacle. They also recommend several chlorophyll-containing substances which, taken by the mouth, almost completely deodorize the colonic contents. In 5 years they have used these methods successfully on 500 patients with permanent colostomies.

MULLEN, W. H. AND MAKIELSKI, L. J.: *The lateral decubitus position in cholecystectomy.* Cleveland Clinic Quarterly, 19, 1, Jan. 1952, 20-27.

The gallbladder is x-rayed with the patient lying on his right side so that the gallbladder drops down and the gas-filled bowel floats up to the left. This usually circumvents the superimposition of gas shadows on the gallbladder and removes the difficulty encountered when the spine obscures the gallbladder. The authors use the method routinely, in addition to a postero-anterior prone film. The method can distinguish between non-opaque stones and multiple papillomata, since the former settle to the bottom of the gallbladder, whereas the latter remain in the same position as seen in the P. A. prone film.

KUROTSU, T., TAKEDA, M. AND BAN, T.: *Studies on the gastrointestinal motility and hemorrhage induced by the hypothalamic stimulation of rabbits.* Med. J. Osaka Univ., 2, 3, Aug. 1951, 97-109.

Obliteration of gastric motility as a result of stimulating the ventromedial hypothalamic nucleus was transmitted through both coeliac ganglia. Increase of gastric motility as a result of stimulation of the lateral hypothalamic nucleus was transmitted chiefly via the vagi. The tone of the rectum was unaffected by either form of stimulation.

BATES, G. S.: *Massive gastrointestinal hemorrhage.* Harper Hosp. Bull., 10, 2, Mar.-Apr. 1952, 41-45.

Massive gastrointestinal hemorrhage from peptic ulcer is an immediate threat to life. That threat lies in anoxia from hemoglobin loss and is remediable. The basis of treatment is prompt, rapid and massive replacement of large amounts of blood lost. Medically uncontrollable bleeding will occur in 10 percent of cases. Successful surgical control of bleeding and of the ulcer in these cases can be obtained in about 90 percent.

COOPER, R. R.: *Definitive treatment for idiopathic ulcerative colitis.* Harper Hosp. Bull., 10, 2, Mar.-Apr. 1952, 45-50.

This is a review of medical treatment and its usual failures, followed by a plea for surgical treatment.

CARPENTER, W. S.: *Colectomy for the cure of ulcerative colitis.* Harper Hosp. Bull., 10, 2, Mar.-Apr. 1952, 50-54.

Total colectomy seems to be a reasonable procedure for the cure of ulcerative colitis which does not respond to medical measures. The operation is not difficult, body metabolism is not deranged and mortality and morbidity are low. With the present requirements in the preparation and cure of an ileostomy fulfilled, the patient who has been cured of ulcerative colitis by colectomy can now be a healthy and happy member of society.

RUBBO, S. D.: *Epidemiology of infectious diarrhea.* Med. J. Australia, Mar. 29, 1952, 425-428.

In 40 to 70 percent of cases of epidemic diarrhea, no organism of known pathogenicity can be detected. The proper classification of gastro-enteritis is as follows—(a) enteritis of known etiology (Salmonella, Shigella, staphyloenterotoxic, Giardia), (b) enteritis of doubtful etiology (proteus, paracolon, coliform, D433, viral), (c) enteritis of anonymous etiology (parenteral, neonatal, non-specific, etc.). "Summer" diarrhea no longer exists. Diarrhea of parenteral origin is relatively uncommon. Thus, we have a common disease with a multiple etiology. Infectious diarrhea is a disease of major importance in infancy. There is an increasing proportion of institutional outbreaks due to Salmonella and Shigella species. Staphylococcal food poisoning (staphyloenterotoxic enteritis) should be given greater consideration because 30 to 50 percent of people are nasal (and hand) carriers of staph. pyogenes. Already good evidence has been produced to show that D433 strain of B. coli is probably responsible for a number of cases of infectious diarrhea in infancy. Further study of this and other coliform bacilli in the intestines of infants is needed.

MCNEISH, W. M. W. AND STEWART, C.: *Outbreak of Bornholm disease in West Fife practice.* Brit. Med. J., Apr. 5, 1952, 744-745.

Bornholm Diseases seem to be an intection of the diaphragm. The infection probably arises in the muscle but may spread to the pleura. The infecting agent is considered to be the Coxsackie group of viruses. Onset is sudden with pain in the upper abdomen or lower thorax. The pain usually is related to breathing. Occasionally pleural friction may be noted. In the 24 cases seen by the authors, the treatment was symptomatic. The disease may last 2 weeks or even longer.

MISSISSIPPI VALLEY MEDICAL SOCIETY 1953 ESSAY CONTEST

The thirteenth Annual Essay Contest of the Mississippi Medical Society will be held in 1953. The Society will offer a cash prize of $100.00, a gold medal, and a certificate of award for the best unpublished essay on any subject of general medical interest (including medical economics and education) and practical value to the general practitioner of medicine. Certificates of merit may also be granted to the physicians whose essays are rated second and third best. Contestants must be members of the American Medical Association who are residents and citizens of the United States. The winner will be invited to present his contribution before the Eighteenth Annual Meeting of the Mississippi Valley Medical Society to be held in Springfield, Ill., Sept. 23, 24, 25, 1953, the Society reserving the exclusive right to first publish the essay in its official publication—the Mississippi Valley Medical Journal (Incorporating the Radiologic Review). All contributions shall be typewritten in English in manuscript form, submitted in five copies, not to exceed 5000 words, and must be received not later than May 1, 1953. The winning essays in the 1952 contest appear in the January 1953 issue of the Mississippi Valley Medical Journal (Quincy, Ill.)

Further details may be secured from

Harold Swanberg, M.D., Sec.
Mississippi Valley Med. Society,
209-224 W. C. U. Building,
Quincy, Illinois.

BARIUM CUP

A specially designed Barium Cup which puts an end to the messy and time consuming mixing and cleanup following the service of barium meals, has just been announced by Ruby Products Company of Milwaukee, Wisconsin.

This 14 oz. Barium Cup, in addition to having an attractive caduceus imprinted on its sides, also has both cubic centimeter and ounce graduations for quick and accurate measurement of contents.

Of sturdy construction, the new Barium Cup allows for the barium meal to be mixed right in it in an electric mixer through the use of a metal collar, also available. Made of heavy grade paper, the cup will not chip, crack or collapse, and is of course, completely disposable, saving washing time and reducing the number of handling operations.

After the barium meal is mixed in the Barium Cup, the cup is placed in a newly developed plastic holder which glows in the dark by virtue of a luminescent band which in no way adversely affects fluoroscopy or X-ray procedures. The barium meal is served right in the Barium Cup.

Also available, Ruby tells us, are two stainless steel dispensers for the new cups. One, a wall model, attaches quickly and easily to almost any surface by means of a simple bracket, and the second is the same dispenser with a desk or table stand base.

Ruby Barium Cups are distributed through several nationally known X-ray supply companies. For the names of these firms, contact Ruby direct.

CAMOQUIN CLEARS MALARIA WITH SINGLE DOSE, INDIAN ARMY PHYSICIANS REPORT

Bombay, India.—A single dose of Camoquin, dihydrochloride dihydrate, cleared a large number of heavily-infected cases of malaria in soldiers within two days, two Indian Army physicians have reported.

Drs. Inder Singh and T. W. Kalyanum of the Indian Army Medical Corps wrote in the British Medical Journal (4779:312, 1952) that the Parke, Davis & Company product proved superior to all other antimalarials in extensive clinical tests. They said that in benign malaria the average duration of fever was 24 hours after administration of Camoquin and 33 hours in malignant malaria. All parasitaemia cleared within 48 hours.

After comparison with other antimalarials, the doctors noted that "one finds a marked diminution in the relapse rate with larger doses of Camoquin. Apparently, this drug is superior in this respect to all other antimalarials and their various combinations."

Adequate dosage was found to be 350 to 400 mg. of Camoquin in benign malaria and about three times that amount in malignant malaria. Adequate concentrations, highest in the spleen, were maintained for a week or more.

"Camoquin was well tolerated by all patients without giving rise to any complaint," the physicians noted. "Blood and urine examinations which were carried out showed no changes. . . . Little or no discoloration of the skin was noted."

The patients were all soldiers between 16 and 35 years old who belonged to the Kolpahur State Forces. They had acquired heavy malarial infections after staying in various endemic or hyperendemic zones of India. None had received any treatment previously.

Conclusions Confirmed By Other Authorities

The Indian Army physicians' conclusions on Camoquin have been confirmed by many other authorities. Among them are two Americans, Drs. L. M. Deane and V. A. Sutter, who administered a single dose of Camoquin to 496 patients in the Amazon region of Brazil in a program sponsored by the Brazilian Ministry of Education and Health in cooperation with the Institute of Inter-American Affairs. In all cases, the physicians reported, fever disappeared before the fourth day after taking a single dose of Camoquin.

Camoquin was introduced by Parke-Davis after an extensive research program started during World War II. Malaria causes the greatest amount of serious illness and the greatest number of deaths of any single disease. Each year more than 350,000,000 people, 13 percent of the earth's population, suffer from malaria.

Camoquin now is available through Parke-Davis branches and distributors throughout the free world.

COURT ACTION

An important court action in the current battle against the substitution evil in the pharmaceutical field is hailed by E. F. Heffner, Jr., vice-president of the A. H. Robins Co., Inc., Richmond, Va., as "an en-

couraging step in the right direction, that is, from mere moral disapproval to definite legal action to halt a dangerous practice."

Mr. Heffner's comment followed the issuance of an order by Federal Judge Edward Weinfeld enjoining a New York company from manufacturing, having manufactured or offering for sale tablets which might be confused with Pabalate, the Robins antiarthritic prescription specialty.

The injunction was granted against "Bonded Laboratories, Inc., Hans Lowey and David Schwartz, the latter individually and trading as Bryant Pharmaceutical Company" on October 31 after a hearing in United States District Court, Southern District of New York (Civil Action No. 77-245).

As a part of the settlement reached at the time the order was issued, the Bryant Co. agreed to cease and desist from manufacture and/or sale of their imitations of three other Robins products.

Early this year Mr. Heffner queried state boards of pharmacy, state pharmaceutical associations and other groups allied with the industry on their attitudes toward substitution. Vigorous opposition to the practice was indicated in the replies. Since then, discussions at various professional meetings have dealt with means of "putting teeth" into existing enforcement procedures, along with the desirability of legislation against the evil in states where none now exists.

BOOKLET ON PLANNING X-RAY PROCESSING FACILITIES AVAILABLE

A new booklet to assist architects and hospital personnel in planning x-ray processing facilities and equipment has just been announced by the Eastman Kodak Company.

The booklet, "Planning the X-Ray Processing Facilities and Equipment," is the first complete compilation of the data published in Medical Radiography and Photography describing processing facilities for x-ray. The material, however, has heretofore been available as a three-part publication of the same name.

The booklet covers planning the general layout, light-tight entrances, electric wiring, ventilation, floor-covering, wall-covering, and illumination, the construction of the loading bench, x-ray processing tanks design, materials, installation and plumbing for x-ray processing tanks, and temperature control for x-ray processing tanks.

Copies of "Planning X-Ray Processing Facilities and Equipment" may be obtained on request to Medical X-Ray Sales Division, Eastman Kodak Company, 343 State Street, Rochester 4, New York.

Mitchel Air Force Base, L. I., N. Y.—The wounded can't take care of themselves! The Air Force Nurse Corps needs 1000 registered nurses to fill critical vacancies in Air Force hospitals throughout the world.

Nurses with the proper qualifications, who are looking for a career with a future, are eligible for a Reserve commission in the United States Air Force. If you are an American citizen, and between 21 and 45, married or single, but with no dependents under 18 . . . then YOU may apply for a challenging future with the Air Force Nurse Corps!

If accepted, you'll train at the School of Aviation Medicine at Gunter Air Force Base, Alabama. Here you'll be taught the application of advanced modern aviation medicine and airborne nursing practices.

You'll also be given an opportunity to specialize. You may become a Staff Nurse, Head Nurse, Preventive Medicine Nurse, Training Consultant, Flight Nurse, Communicable Disease Nurse, or specialize in Pediatrics, Operating Room techniques, Obstetrics, Neuropsychiatrics, and Anesthetics. There is no limit to the opportunity for advancement and training with the Air Force Nurse Corps.

Financial and professional security are some of the many advantages offered Air Force nurses. Good pay . . . over $300 per month for Second Lieutenants, educational opportunities, and veteran's benefits are only part of the picture. For further information about the Air Force Nurse Corps, write to the Chief Nurse, Headquarters, First Air Force, Mitchel Air Force Base, New York.

X-RAY STUDY OF BILE DUCTS MADE POSSIBLE WITH TELEPAQUE

Clinical study of the bile ducts, simultaneous with visualization of the gallbladder, has been effectively accomplished with the new contrast medium Telepaque, according to Drs. Robert M. Bowman and H. W. Stanley of Grace-New Haven Community Hospital, New Haven, Conn.

They report that this development makes "preoperative cholangiography possible."

In the treatment of gallbladder disorders, the doctors state in the Connecticut State Medical Journal (16:591, 1952), the ability to view the common and cystic ducts provides valuable confirmation of the normal function of the gallbladder and sphincter of Oddi. Previously, such confirmation had been obtained through surgery.

Visualization of the ducts was successful in more than 50 per cent of 350 cases studied by the investigators subsequent to the completion of their preliminary report of 100 cases. The latter study evaluated the incidence of symptoms and diagnostic results obtained with Telepaque and a second commonly-used contrast agent.

Fewer and less severe symptoms were experienced with Telepaque, the doctors state. Fifty-eight per cent showed no side reactions as compared with 33 per cent tested with the second compound, including a significant reduction in the incidence and intensity of dysuria.

The density of the shadow of the gallbladder was "definitely greater" following use of Telepaque, which was also found to be helpful in viewing opaque calculi. Drs. Lowman and Stanley further note that there was no adverse physiologic response of the gallbladder to a fatty meal, and concludes with the observation that "Telepaque offers definite advantages as a cholecystographic medium."

Winthrop-Stearns Inc. supplied Telepaque in 0.5 Gm. tablets.

HONORS

E. Claiborne Robins, president of A. H. Robins Co., Inc., Richmond, Va., pharmaceutical house, has been elected to membership in Omicron Delta Kappa, national hon-

orary leadership fraternity. He was the only University of Richmond alumnus to be so honored this year. A member of the class of 1931, Mr. Robins is now president of the Richmond Chamber of Commerce and a member of the board of trustees and athletic council of the university. He was graduated from the Medical College of Virginia in pharmacy in 1933 and is a member of the Kappa Psi pharmaceutical fraternity.

REDUCING AID

Did you ever try to "walk off" extra weight? To lose two pounds that way, the average person must walk ten extra miles a day for a week without increasing the food intake, according to Dr. Norman Joliffe, nutrition chief of the New York City health department. The same result can be obtained by eating daily for one week 1,000 calories less than is used up. As a means of keeping patients on their prescribed diets, Dr. Joliffe instructed a sample group to take a four-ounce glass of orange juice or grapefruit juice half an hour to an hour before the noon meal and the evening meal. This acted as an appetite-appeaser, leading to "a high degree of adherence to the prescribed regimen" with gratifying weight losses.

KEEP ORANGE JUICE IN REFRIGERATOR

Unlike bananas, reconstituted frozen orange juice belongs in the refrigerator. Placed there, at 40 degrees Fahrenheit, "vitamin C losses will be negligible," states the Council on Foods and Nutrition of the American Medical Association. Vitamin losses occur when the reconstituted juice is allowed to stand in an open container at room temperature. According to the Council, "it is reliably estimated that approximately 98 percent of the vitamin C content of the fresh fruit may be retained in the frozen concentrated juice when modern acceptable methods are used."

HOW TO SQUEEZE BABY'S ORANGE JUICE

"Orange juice, when extracted without undue pressure being made on the orange peel, is well tolerated by infants and children and allergic reactions are minimal," report Drs. C. L. Joslin and J. E. Bradley of the University of Maryland Department of Pediatrics after testing 406 young patients. Of these, 224 were in two infant homes. One institution was well satisfied with the results of fresh orange juice. The other reported trouble with regurgitation and skin rashes. Investigation soon disclosed the reason for this difference. The first institution was using an extractor of the Mixmaster type, the second a mechanical extractor which exerted heavy pressure on the skin of the halved orange and mixed orange peel oil freely with the juice. Skin tests given to a group of babies showed 5.3 percent allergic to peel oil, while 98.2 percent gave no reaction to orange juice. Frozen orange juice concentrate, and juice extracted without pressure upon the peel, were found to be the most desirable forms.

FROZEN ORANGE JUICE "NUTRITIVE EQUAL" OF FRESH

Frozen concentrated orange juice made from properly selected and prepared fruit is a dependable source of vitamin C and may be useful in the diets of persons of all ages, states the Council on Foods and Nutrition of the American Medical Association. "In fact," says the Council report, "it may be considered as the nutritive equal of fresh orange juice. Thus, it will meet the need for Vitamin C intake in the diets of all persons, including infants."

PRIZE FOR PAPER ON DIABETES BY MEDICAL STUDENTS AND INTERNS

The American Diabetes Association offers a $250.00 prize to *medical students* and *interns* for a paper on any subject relating to diabetes. The paper can be a report of original studies, a biographical or historical note, a case report with suitable comment, or a review of the literature.

This incentive is particularly apropos in the field of diabetes, since Dr. Paul Langerhans made his studies of the pancreas, describing the islets that bear his name, while he was an undergraduate student in Berlin in 1869; and Dr. Charles H. Best, while a graduate student was co-discoverer of insulin in 1922.

Manuscripts must be submitted on or before April 1, 1953 to the Editorial Offices of Diabetes: The Journal of the American Diabetes Association, 11 West 42nd Street, New York 36, New York. The papers will be reviewed by the Editorial Board, which will take into consideration the value of the material and method of presentation in selecting the best paper.

The award of $250.00 has been made possible through the generosity of the St. Louis Diabetes Association, an Affiliate of the American Diabetes Association.

PARKE-DAVIS SCIENTIST TO DISCUSS USES OF ATOMIC ENERGY IN MEDICINE AND PHARMACY

New York.—Uses of atomic by-products in medicine and pharmacy were discussed by Dr. D. A. McGinty, laboratory director in physiological research of Parke, Davis & Company, in a round table on atomic energy in industry sponsored by the National Industrial Conference Board in New York City Oct. 16 and 17.

Dr. McGinty, a nationally-recognized authority on atomic energy in medicine, reviewed aspects of the use of atomic tracers and isotopic materials in research, emphasizing factors of costs, efficiency and quality of results.

Parke-Davis was among the first to use atomic by-products in medical and pharmaceutical research. Radioactive isotopes were being used in Parke-Davis laboratories as early as during World War II, even before their availability from the Oak Ridge (Tenn.) National Laboratories.

Others on the round table on atomic energy in medicine and pharmacy with Dr. McGinty included: Dr. Charles L. Dunham, Chief, Medical Branch Division of Biology and Medicine, Atomic Energy Commission; D. L. Tabern, Abbott Laboratories; C. Rosenblum, Merck and Co.; Bernard Roswitt, U. S. Veterans Administration Hospital, the Bronx, New York; and Dr. Edith Quimby, Columbia University Medical School.

Principal speakers on the two-day program, covering discussions of atomic energy in all branches of industry, were David Lilienthal, former chairman of the U. S. Atomic Energy Commission; T. Keith Glennan, present member of the Commission; and Philip Sporn, president of the American Gas and Electric Service Corporation.

Dr. McGinty has been associated with Parke-Davis research for 19 years. Prior to that, he received his bachelor's degree from the University of Denver, his master's degree from the University of Illinois, and his Ph.D. from the University of Michigan.

ROBINS CO.

Dr. Eugene L. Jackson, medical director of the Richmond, Virginia, pharmaceutical firm of A. H. Robins Co., Inc., addressed the 1952 convention of the Illinois Academy of General Practice held in Peoria, Ill., October 21, 22 and 23.

A former professor of pharmacology and department chairman at Emory University School of Medicine, Dr. Jackson Spoke on "Pharmacology as Related to Medical Practice."

According to Dr. Jackson, the science of pharmacology has exerted a great influence on medical practice particularly in the fields of diagnosis and therapy. As drugs with increasing specificity of action have been and continue to be developed, more and more accurate diagnoses and more effective treatment become possible. At the same time, however, increased specificity of action is often accompanied by an increased possibility of harmful effects on the patient. Both the pharmacologist and the physician, therefore must assume the added responsibility of continual care in the selection and use of these drugs.

NAMED CANCO DIRECTOR

Donald B. Kipp, member of the law firm of Pitney, Hardin & Wood, of Newark, N. J., has been elected a director of American Can Company.

Mr. Kipp, a graduate of Princeton University and Harvard Law School, also is a director of the American Colortype Co., American Insurance Co., and the Bankers Indemnity Co. He resides on Spring Valley Road in Morristown, N. J.

AMERICAN PHARMACEUTICAL ASSOCIATION ELECTS JOHN A. MACCARTNEY, PARKE-DAVIS TRADE RELATIONS MANAGER, AS FIRST VICE-PRESIDENT

Detroit.—John A. MacCartney, trade relations manager of Parke, Davis & Company, has been elevated to first vice president of the American Pharmaceutical Association.

The 47-year-old executive will be installed with other new officers at the annual convention in Salt Lake City the week of Aug. 16. He has served during the past year as second vice-president of the association, which represents approximately 30,000 pharmacists throughout the United States. It is the oldest such organization of its kind.

As trade relations manager of Parke-Davis, MacCartney makes more than 100 speeches before professional groups across the country each year. He also supervises the pharmaceutical firm's unique plant tours, which attract over 10,000 persons annually. The visitors, who pay their own expenses to and from Detroit for the privilege of walking 10 miles through the Parke-Davis laboratories, are connected directly or indirectly with the pharmaceutical industry — practicing physicians, pharmacists and dentists; hospital internes and resident doctors; and upperclassmen from schools of medicine and pharmacy.

A native of Claysville, Pa., MacCartney was graduated from the College of Pharmacy at the University of Pittsburgh in 1928 and almost immediately joined Parke-Davis. During World War II, he served with the U. S. Army medical corps in the Pacific and was in charge of medical supply during the first occupation of Korea in 1945. He rejoined Parke-Davis in June, 1946, and soon afterwards was promoted to trade relations manager.

MacCartney lives at 917 University, Grosse Pointe, Mich., a Detroit suburb.

Nutley, N. J. — Hoffmann-La Roche Inc., has just introduced Granti*cillin* "Roche" which provides the combined antibacterial action of Gantrisin—the highly soluble, single sulfonamide— and penicillin G. Each Gantri*cillin* tablet contains 0.5 Gm of Gantrisin and 100,000 units of penicillin G potassium.

Numerous published reports have described the effectiveness of Gantrisin as an antibacterial agent when used alone and in combination with penicillin. In serious infections, combined Gantrisin-penicillin therapy is frequently recommended. Gantri*cillin* provides Gantrisin plus penicillin in a convenient oral form. The new Gantri*cillin* tablets are now available in bottles of 24, 100 and 500.

GASTRIC ANACIDITY

An effective, accurate method for detecting gastric anacidity in cases of suspected stomach cancer, pernicious anemia or gastric polyps, without submitting the patient to the discomfort of intubation, is offered by Diagnex (Squibb Quinine Carbacrylic Resin), recently made available by E. R. Squibb & Sons.

Diagnex is an ion exchange resin in the form of an insoluble powder. When swallowed in a glass of water by the patient the quinine in Diagnex is displaced by the hydrogen ions of the free hydrochloric acid normally present in the stomach. Fifteen to twenty per cent of the displaced quinine is excreted in the urine within two hours. Thus a simple urine assay for the presence or absence of quinine indicates the presence or absence of free hydrochloric acid in the stomach.

The test for gastric anacidity afforded by Diagnex is extremely valuable in the diagnosis of pernicious anemia, gastric polyps and stomach cancer, since gastric anacidity is commonly associated with these conditions. Although a final diagnosis cannot be made on the basis of this test alone, it provides a useful method for screening out patients with minor complaints from those who need further study.

Diagnex is packaged in a match-folder type unit incorporating the quininium resin, a capsule of caffeine sodium benzoate to stimulate gastric secretions, three labels for urine collection bottles and a set of simple instructions to the patient.

Directions for making urine determinations will be supplied automatically to hospitals and private laboratories and to individual physicians upon request.

Meat...

and Its Important Contribution of Essential Amino Acids

Although the daily allowance of protein recommended for human beings has been established for some time,[1] only very recently has a recommended daily intake of individual essential amino acids been proposed.[2] These new criteria now give a more accurate means for nutritionally evaluating the protein contribution of meat than was possible just on the basis of the gross amount of protein meat provides.

The table which follows gives the proportions of the recommended daily intake of individual essential amino acids provided by six ounces of cooked meat, the approximate average per capita daily consumption in the American diet. Note that though furnishing about 52 per cent of the daily protein allowance for a normal adult male, six ounces of meat supplies more than the recommended daily intake for a majority of the essential amino acids and a goodly proportion of the recommended intake of the remainder.

Percentages of Recommended Daily Intake of Eight Essential Amino Acids and of Protein Contributed by 6 Oz. of Cooked Meat*

Essential Amino Acids	Beef[3]	Lamb[4]	Pork[4]
L-Isoleucine	141	121	127
L-Leucine	150	120	125
L-Lysine	202	163	172
L-Methionine	42	34	40
L-Phenylalanine	70	63	70
L-Threonine	160	169	183
L-Tryptophan	90	90	100
L-Valine	136	107	113
Protein	56	49	51

*In the calculations, averages of the percentages of protein in six different cuts of each type of cooked meat were used, as were averages of the percentages of the amino acids in the protein of the respective cuts.

Every kind and cut of meat is not only an excellent source of the essential amino acids but also of the nonessential amino acids, the B group of vitamins, iron, and other essential minerals. Morever, meat is rapidly and almost completely digested, has a stimulating influence upon appetite and digestion, and gives a gratifying sense of satiety. All these nutritional and physiologic advantages of meat fully justify its prominent place in normal diets of persons of all ages and in many special diets.

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2. Rose, W. C.: Half-Century of Amino Acid Investigations, Chem. and Eng. News *30*:2385 (June 9) 1952.
3. Greenwood, D. A.; Kraybill, H. R., and Schweigert, B. S.: Amino Acid Composition of Fresh and Cooked Beef Cuts, J. Biol. Chem. *193*:23 (Nov.) 1951.
4. Schweigert, B. S.; Guthneck, B. T.; Kraybill, H. R., and Greenwood, D. A.: The Amino Acid Composition of Pork and Lamb Cuts, J. Biol. Chem. *180*:1077 (Oct.) 1949.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.

FRUIT SUGARS IN LOW-CALORIE DIETS

Some patients are obese and hypoglycemic at the same time. While needing to take off weight, they must at the same time be on guard against a deficiency of sugar in the blood. Replying to a doctor's query in the Journal of the American Medical Association, an authority states that the diet for an overweight patient with hyperinsulinism (spontaneous hypoglycemia) should be low in carbohydrates and high in proteins, with a limited amount of fats. "Fruit or fruit juices (orange, apple, or grapefruit) should be taken for breakfast, every two or three hours between meals, at bedtime, and, if awake, during the night," the answer adds.

PARKE, DAVIS & CO. ANNOUNCES SIX PROMOTIONS, MADE NECESSARY BY EXPANDING DOMESTIC AND OVERSEAS ENGINEERING REQUIREMENTS

Detroit.—Thomas C. Anderson, director of production and engineering for Parke, Davis & Company, today announced six promotions which were "made necessary by the expanding requirements of our domestic and overseas engineering activities."

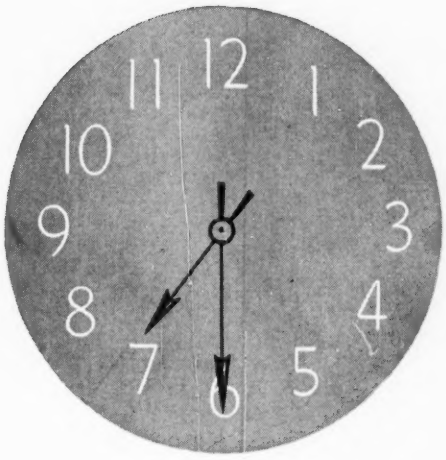
William H. Mohrhoff, 41, was elevated to assistant director of overseas liaison and will handle engineering and production problems of overseas operations requiring home office attention. A native of Pittsburgh, Mohrhoff majored in chemical engineering at the University of Michigan and graduated in 1934. He joined Parke-Davis that year, served in various engineering and production capacities and became superintendent of the antibiotics division in 1946, holding that post until his present promotion. Mohrhoff lives at 11832 Kilbourne Street, Detroit.

William G. Meier, 37, a native of Beacon, N. Y., was elevated to assistant director of engineering and will be responsible for all engineering and maintenance connected with the pharmaceutical firm's U. S. and Canadian operations. A graduate of New York University and a registered mechanical engineer, Meier joined Parke-Davis in February, 1952, as superintendent of engineering and maintenance. He lives at 3955 Bishop, Detroit.

Edwin F. Lau, 30, was promoted to superintendent of the antibiotics division. Born at Pleasant Ridge, Mich., Lau was graduated from the University of Michigan in 1947 with an M.S. degree in chemical and metallurgical engineering. He served with the U. S. Naval Reserve during World War II, joined Parke-Davis in 1947, had several promotions and was elevated to his new post from assistant superintendent of the antibiotic division. He formerly was president of the Junior Section, Engineering Society of Detroit, and lives at 2305 North Wilson, Royal Oak, Mich.

Thomas E. Harris, 43, who joined Parke-Davis in 1933, was elevated to superintendent of construction and maintenance. A 1933 graduate of the University of Michigan, with an M.S. in mechanical engineering, Harris was in charge of the capsule engineering department from 1939 until 1949, when he was transferred to the construction and maintenance division. He is a Detroit native, belongs to the Engineering Society of Detroit and lives at 1494 Bewick Avenue, Detroit.

Dow K. Foraker, 50, who has



habit time

● Habit Time of Bowel Movement—not merely relief of constipation—is secured by proper use of Petrogalar.

Petrogalar promotes development of normally hydrated, comfortable and easily passed stools.

Once achieved, the normal bowel habit may often maintain itself even though the dosage of this adjuvant is slowly tapered off.

PETROGALAR®

AQUEOUS SUSPENSION OF MINERAL OIL, PLAIN

Supplied: Bottles of one pint

Wyeth®

been with the firm since 1934, was promoted to superintendent of engineering. A 1925 graduate of Tri-State College, Angola, Ind., Foraker has spent his entire Parke-Davis career in the engineering department. He is a native of Bippus, Ind., and lives at 6155 Bluehill, Detroit.

Herve H. Hunt, 32, was promoted to assistant superintendent of engineering. Born at Oxford, Miss., Hunt studied mechanical engineering at Michigan State College and was graduated in 1943. He joined Parke-Davis almost immediately, but left to attend the U. S. Navy radar schools at Princeton and M.I.T. and serve during World War II as a submarine officer. He returned to the firm in 1946, studied electrical engineering at Wayne University and was graduated in 1950. A member of the Engineering Society of Detroit and the American Society of Mechanical Engineers, he is a registered mechanical and electrical engineer. Hunt lives at 12273 Longview, Detroit.

JUSTICE AND THE ORANGE

There is a story told of the late Chief Justice Hughes, that in order to retain his erect, youthful carriage, he practiced walking around a room for fifteen minutes a day with an orange balanced on his head.

The Justice, as usual, was right. Whether by this exercise or by sheer will power, he kept his head unbowed. Perhaps even more beneficial would have been the internal use of the orange. For in the new science of geriatrics—care of the aged—orange juice is an important source of an essential vitamin. Dr. I. W. Winfield writes in Nursing Home Administrator that orange juice is recommended by specialists in geriatrics for increasing the fluid intake of older persons, and for raising the low vitamin C reserve that is characteristic in aged people. Citrus fruits are also found to have a stimulating effect on the digestive glands, so that they are particularly helpful to people of advanced years who have little appetite for food. Without some stimulus, such people tend to consume an inadequate diet, but citrus fruits both provide essential vitamins themselves and help to awaken the desire for other necessary foods.

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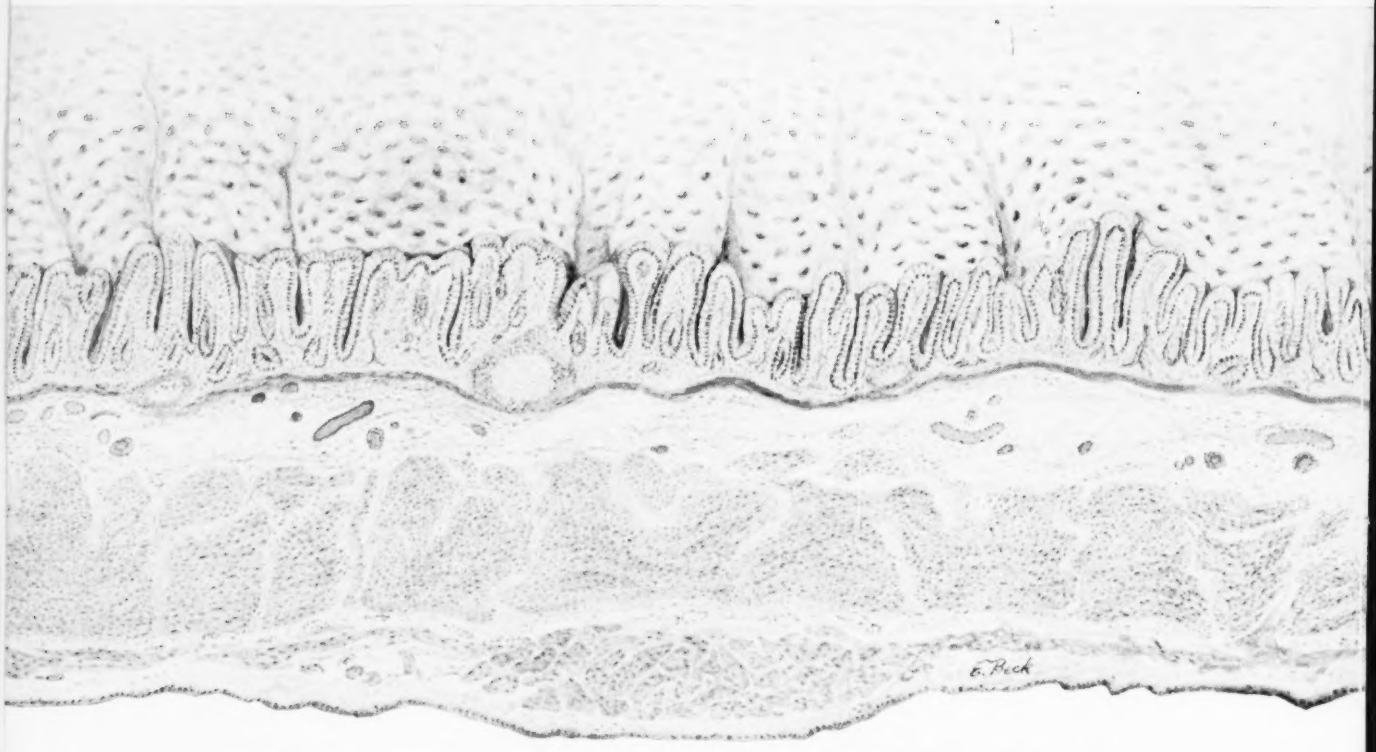

Normal peristaltic action results from activity of the muscle layers as they are gently distended by bulk within the intestine; mucosal irritants cause overactivity of the muscle layers resulting in hyperperistalsis or spasm.

Corrective Action of Metamucil® in Abnormal Physiology of Constipation

Abnormally prolonged colonic retention, whether in a spastic or an atonic colon, demands the greatest care to assure correction.

The mucosa does not require stimulating; hence, stimulating cathartics, "roughage" and other physical and chemical irritating measures, are today often considered irrational.

On the other hand, the muscularis does require a stimulus to initiate peristalsis. This physiologic stimulus is the mechanism by which bland distention of the colon establishes a reflex, with the muscularis at the terminus of the reflex arc.

Metamucil literally reeducates the sluggish and also the spastic colon. Taken with adequate amounts of water, Metamucil forms a smooth, hydrophilic colloid. As this colloidal mass passes through the large intestine, it exerts a gentle, distending pressure within the lumen, thus initiating the peristaltic reflex necessary for evacuation.

A program of Metamucil therapy helps to restore proper tone to the intestinal musculature, thereby establishing proper bowel habits.

Metamucil® is the highly refined mucilloid of Plantago ovata (50%), a seed of the psyllium group, combined with dextrose (50%) as a dispersing agent. It is accepted by the Council on Pharmacy and Chemistry of the American Medical Association.

G. D. Searle & Co.

Research in the Service of Medicine